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## A NEW METHOD OF PYLOROPLASTY.

By J. M. T. Finney, M. D.,

*Associate Professor of Surgery, Johns Hopkins University.*

The first plastic operation for the relief of a benign stricture of the pylorus was performed by Heineke in eighteen hundred and eighty-six. A few months later Mikulicz made use of exactly the same procedure, being at the time in ignorance of the work of Heineke. This operation has since borne the names of these two surgeons.

Before discussing the relative advantages and disadvantages of their particular method, a word or two, concerning other operative procedures designed to accomplish the same result, will not be out of place.

The methods used in the treatment of non-malignant stricture of the pylorus, seem, all of them, open to certain special objections. Digital or instrumental divulsion of the pylorus, whether by the method of Loreta or Hahn, has proven very unsatisfactory as judged both by immediate risks and final results, and has been practically abandoned.

Jaboulay, in eighteen hundred and ninety-two, proposed the operation of gastroduodenostomy. Modifications of this method have been suggested by Duranti and Henle, but it has never met with much favor on the part of the profession. This operation I performed three years ago, in a case of pyloric stricture from old ulcer. The condition of the patient, an old lady, has been improved but not entirely relieved. It was the partial failure in this case that led me to seek a better method.

The operation of pylorectomy, on account of the greater technical difficulties and increased danger in its performance, must of necessity remain of limited usefulness. Theoretically, of course, it is the ideal operation, but practically, except in rare instances, malignant disease is its sole indication.

Gastroenterostomy, devised by Nicoladoni in eighteen hundred and eighty-one, seems at the present time to be the operation of choice with the majority of surgeons, and the weight of surgical authority is decidedly in its favor.

But as to the relative merits or demerits of this operation, performed by whatever method, there still exists among surgeons, great diversity of opinion. Call it by whatever name you will, explain it as you may as being due to the reflux of bile into the stomach, or as resulting from the presence, in the duodenum, of particles of partially digested food, the fact remains that the "Circulus viciosus" of the Germans is present in a not inconsiderable percentage of cases, and when it does occur, it is productive of much discomfort to the patient, and is a grave menace to the success of the operation.

While it is undoubtedly true, that for some reason or

other, this percentage varies much in the hands of individual operators of large experience, still in the aggregate, the danger and suffering from this source are so great as to make it well worth while to eliminate it altogether, if it were possible. The great desideratum, of course, is to establish an opening between the stomach and bowel which will remain patulous and through which, at the same time, the bile and stomach contents will not tend to regurgitate.

From a careful study of the subject, it would seem that the Heineke-Mikulicz operation, while having in selected cases definite advantages over any other operation, still has certain recognized objections. Attempts to overcome these defects have been made by several operators. Richardson, of Boston, advocates an oval or diamond-shaped incision through the pylorus, which accomplishes the excision of the anterior portion of the stricture and leaves only the posterior wall as a hinge upon which the duodenum and stomach are brought together. Mayo Robson speaks with favor of this method, and Morrison has recently reported several cases in which he has made use of the same procedure with success. Koeppelin and Jaboulay recommend what they call "sub-mucous pyloroplasty," in which the incision is carried down to but not through the mucosa. The divided serous, muscular and sub-mucous coats are then united in the usual way. They maintain that this modification is safer than the original method, the danger of sepsis being done away with. Enough cases, however, have not been reported to determine its usefulness, and it would seem, theoretically, at least, of doubtful utility. Mayo Robson advocates the use of an "internal splint in the shape of a bone bobbin over which to apply the sutures," a method, which, he states, has been employed in all his operations, and one which offers several advantages, for instance: "Only two continuous sutures are required, for the mucous and peritoneal margins respectively. The bone tube secures an immediate and thoroughly patent channel which affords protection for from twenty-four to forty-eight hours to the line of sutures, by which time union should be established. And it prevents the new channel being inadvertently made too narrow." This modification has been followed by other surgeons with success.

The operation which I propose is practically a modification of the method of lateral anastomosis suggested by Dr. Halsted. I have performed the operation five times. In all of my cases the pylorus was more or less adherent to the surrounding structures, abdominal wall, liver, gall bladder, omentum, and colon. In all the cases, the operation was carried out, notwithstanding the adhesions and thickened walls of the pylorus and stomach with entire satisfaction, and in four cases the result has been complete relief from all unfavorable symptoms. The fifth case has been operated upon too recently to judge as yet as to the result; but so far, he has been entirely relieved of his trouble, eats anything and is gaining steadily in weight. The operation is as follows:

Divide the adhesions binding the pylorus to the neighboring structures, also free as thoroughly as possible, the pyloric end of the stomach and first portion of the duodenum. Upon the thoroughness with which the pylorus, lower end of the stomach, and upper end of the duodenum, are freed, depends, in large measure, the success of the operation, and the ease and rapidity of its performance. I wish to emphasize this as one of the most important points in the operation. Frequently, at first sight, the pylorus may seem hopelessly bound down, when after a little patient toil and judicious use of the scalpel and blunt dissector, it is found that it can be freed with comparative ease. A suture, to be used as a retractor, is taken in the upper wall of the pylorus, which is then retracted upwards. A second suture is then inserted into the anterior wall of the stomach, and a third into the anterior wall of the duodenum, at equidistant points, say about 12 cm., from the suture just described in the pylorus. These second sutures mark the lower ends of the gastric and duodenal incisions, respectively. They should be placed as low as possible in order that the new pylorus may be amply large. Traction is then made upwards on the pyloric suture, and downwards in the same plane, on the gastric and duodenal sutures. This keeps the stomach and duodenal walls taut, and allows the placing of the sutures with greater facility than if the walls remained lax. See Fig. 1. The peritoneal surfaces of the duodenum and stomach, along its greater curvature, are then sutured together, as far posteriorly as possible. See Fig. 2. For this row I would recommend the use of the continuous suture, as it is more easily and quickly applied, and it can be reinforced after the stomach and duodenum have been incised. After the posterior line of sutures has been placed, an anterior row of mattress sutures is taken, which are not tied but left long, in the manner indicated in Fig. 3. These sutures, after they have been placed, are retracted vertically in either direction from the middle of the portion included in the row of sutures. See Fig. 4. Then after all the stitches have been placed and retracted, the incision is made in the shape of a horseshoe. The sutures should be placed far enough apart to give ample room for the incision. The gastric arm of the incision is made through the stomach wall just inside the lowest point of the line of sutures, and is carried up to and through the pylorus and around into the duodenum, down to the corresponding point on the duodenal side. Hemorrhage is then stopped. It is well to excise as much as possible of the scar tissue upon either side of the incision in order to limit, as far as possible, the subsequent contraction of the cicatrix. This procedure I carried out in two of my cases with great satisfaction, and I should strongly recommend it in all cases where the walls of the pylorus are much thickened and there is much scar tissue present. It is well, too, to trim off with scissors redundant edges of mucous membrane, in order to prevent the formation of a valve-like fold of mucous membrane at the new pylorus. A continuous catgut suture is now taken through and through all the coats of the intestine on the posterior side of the incision. See Fig. 5. This reinforces the posterior line of

sutures, secures better approximation of the cut edges of the mucous membrane, and prevents the reunion of the divided intestinal walls. The anterior sutures are then straightened out and tied, and the operation is complete, unless one wishes to reinforce the mattress sutures with a few Lembert stitches. See Fig. 6. This procedure, as is readily seen, gives the minimum of exposure of infected surface. All the stitches are placed and the posterior row tied, before the bowel is opened, and it remains open just long enough to control the hemorrhage. The size of the newly-formed pyloric opening is limited in this operation, only by the mobility of the stomach and duodenum, and the judgment of the operator. In all of my cases the incision has been about 12 cm. in length, and could have been made longer, had I chosen to make it so. Unless the stomach is very much dilated or has descended to an unusual extent, the lower limit of the new outlet is at or near the level of its most dependent portion.

When the stomach is much dilated, there is no contra-indication in this operation to the performance, at the same time, of gastropexy or gastroplication, if one considers them indicated.

In the matter of mortality, statistics, notoriously unreliable in cases of this sort, seem to slightly favor pyloroplasty as against gastroenterostomy. But, nevertheless, the latter operation numbers among its staunchest advocates some of the foremost names in the surgical world. Furthermore, it cannot be denied that during the past few years the operation of pyloroplasty has fallen somewhat into disfavor, partly because of the number of recurrences following it; and partly because of the improved methods recently introduced, and the increased facility in performing the operation of gastroenterostomy. Mechanical devices, such as the Murphy button and the bone bobbin of Mayo Robson, have contributed not a little to the accomplishment of this result. The range of usefulness of gastroenterostomy is, of course, much wider than that of pyloroplasty, which obviously must be restricted to cases of benign stricture of the pylorus. Although Morrison reports a case of early carcinoma of the pylorus treated in this way through mistaken diagnosis, with a result quite as satisfactory as that usually obtained by more radical methods.

The especial objections that have been urged against the Heineke-Mikulicz operation are:

(1) Its inapplicability in cases of extensive and firm adhesions about the pylorus.

(2) Its inapplicability in the presence of still active ulceration.

(3) The liability to recurrence of the stricture due to contraction of the scar.

(4) The inability to obtain good apposition on account of rigidity of the walls of the stomach and duodenum.

(5) The outlet of the stomach is not placed at the most dependent portion, hence in the presence of motor insufficiency the aid of gravity in emptying the stomach is lost.

The effect of some of these objections to the operation is lessened by the modifications suggested by Richardson, Morrison, and others, to which reference has already been made, but the validity of the others has been established by repeated observations.

I believe that all of these objections, with the possible exception of the second, viz: still active ulceration, are overcome by the method here suggested. I am convinced that adhesions, however firm or extensive, constitute no bar to this operation. With care and perseverance they can be separated. If the new pylorus is made sufficiently large, the danger of subsequent contraction is reduced to a minimum. Excision of the anterior portion of the thickened pylorus, and if necessary, the adjacent portions of the gastric and duodenal walls, lessens materially the danger of subsequent contraction, and at the same time allows of easy approximation of the two surfaces.

In an extremely interesting monograph by Carle and Fantino, the functional results following the operations of gastroenterostomy and pyloroplasty are compared. Robson summarizes their findings briefly as follows:

"Points in favor of pyloroplasty:

(1) Regurgitation of bile into the stomach is prevented.

(2) Secretion of hydrochloric acid, when it has been excessive, becomes normal.

(3) If the secretion of hydrochloric acid has been diminished or absent before the operation, it remains in statu quo after operation.

(4) If there has been primary gastric atony, peristalsis is but little improved.

(5) This function improves rapidly or reaches perfection if the muscular contractility has been normal or increased, and when the obstruction was due to fibrous stenosis or pyloric spasm.

(6) In all such cases evacuation of the stomach is accomplished in its physiological period. Only in rare cases, and these only in the first months after operation, may it be delayed.

(7) The capacity of the stomach always decreases, but rarely becomes as small as normal.

(8) The pylorus recovers tone.

Points of difference between the results of pyloroplasty and gastroenterostomy:

(1) The absence of regurgitation of bile, and hence the absence of any biliary influence on the gastric secretions.

(2) The evacuation of the stomach is not accelerated; hence the difficulty the stomach has in reaching its normal size.

(3) The slight or negative result obtained by pyloroplasty in obstruction from primary gastric atony compared to the positive results from posterior gastroenterostomy."

A word as to the preparation of patients for this operation.

Accumulated clinical experience has proven that it is unnecessary and often harmful, to put patients through a long course of preliminary treatment. The observations of Cushing in the Johns Hopkins Hospital, upon the bacteriological examination of the stomach contents, show that

cleansing the mouth and teeth carefully with antiseptic washes and the administration of sterile food only, will quickly render the stomach contents innocuous. The treatment carried out in all of my cases was as follows:

For two or three days before the operation the mouth and teeth were carefully cleansed with carbolic solution and only sterile liquid food and water administered. The stomach was irrigated night and morning, just before operation, with boiled water. No food at all was given by mouth for the twelve hours preceding operation. Cultures were taken from the stomach contents in three of the cases and two were found to be sterile. The skin preparation is the same as for all abdominal cases. I prefer the incision through the right rectus muscle, and make it sufficiently long to give abundant room, say six to eight inches. The greatest care is exercised in protecting the abdominal cavity from soiling by extravasated stomach contents, by the liberal use of Mikulicz' pads of sterile gauze. In two cases Schleich's solution and one per cent solution of cocaine were made use of, but ether had to be substituted in small quantity toward the close of the operation. The abdominal wound is closed without drainage. Nothing is given by mouth for the first thirty-six to forty-eight hours. Enemata of salt solution and coffee are given every five hours, for the first twenty-four hours, after which time nutritive enemata are alternated with the salt solution. Water in small quantities is allowed early. On the second or third day albumin in teaspoonful doses is administered, and if borne well, broths and milk are rapidly added.

Patients, particularly weak ones, are not required to lie flat on the back, but are encouraged to turn and even allowed to be propped up in bed very soon after the operation.

*Case I.*—Miss Emily P., referred to me by Dr. Dunott, of Baltimore, a student, aged twenty-one, entered the Union Protestant Infirmary February 23, 1901, complaining of "stomach trouble." Her family history is negative. She had always been healthy until her present illness began two and one-half years ago as an attack of indigestion which culminated in a severe attack of nausea and vomiting which lasted for some days. Since that time she has always had more or less abdominal distress, has seen many physicians, with little or no relief.

Her attacks seemed at times to be aggravated by partaking of food; at other times, not.

Vomiting was copious and severe; nausea almost constant. She has never vomited blood except after the use of the stomach tube.

Has lost about fifteen pounds recently, looks pale, anæmic, and somewhat emaciated.

Heart and lungs normal. Abdomen slightly distended. Stomach tympany greatly increased. Succussion pronounced. Palpation negative except slight tenderness and muscle spasm over the right hypochondrium.

Patient had been operated upon about three months previously by Dr. Dunott. The abdomen had been opened, some induration was found about the pylorus, the gall bladder was adherent to it. There was a scar, apparently of an old ulcer, in the anterior wall of the stomach near the pylorus and the anterior wall of the pylorus was folded upon itself, making a partial stricture.

The adhesions were separated, and the pyloric wall unfolded as much as possible, when the stricture of the pylorus seemed to be relieved. The stomach was not opened. There was a second scar, also, in the anterior wall of the stomach near the pylorus. Her abdominal wound was closed without drainage. She made a good recovery from the operation, but experienced little or no benefit from it and returned, as before stated, about three months later, for a radical operation.

On opening the abdomen, it was found that the omentum was very adherent to the pylorus and to the scar of the previous operation. The gall bladder was also very firmly adherent to the pylorus and duodenum. The stomach was found to be greatly dilated and scars of old ulcers were apparent near the pylorus. The pylorus, itself, was found much thickened. After freeing all the adhesions, an anastomosis between the stomach and duodenum was accomplished. The pylorus was found to be much contracted, the orifice being less than 1 cm. in diameter.

She made an excellent recovery and reported a few days ago that since the operation, she has been absolutely free from any of her former trouble. At an examination, a few weeks ago, the stomach had diminished to about the normal size. She has gained markedly in weight.

*Case II.*—Mrs. Anna S., aged fifty-five, entered the Union Protestant Infirmary March 16, 1901, referred to me by Dr. J. Friedenwald, of Baltimore, complaining of indigestion and "stomach trouble."

Family history negative. Her trouble dates back about a year. Symptoms have been very severe for about six months past, during which time nausea, vomiting, constipation, and loss of weight have been very pronounced.

She has never vomited blood. Has been unable to eat anything but liquid food, milk, and crackers. Vomits frequently large quantities. Her only relief is from the daily use of the stomach tube. She has lost forty pounds in the last six months.

Examination of the patient shows an exceedingly emaciated, somewhat anæmic looking woman. Heart and lungs negative. Abdomen considerably enlarged. Liver dullness normal. Stomach tympany much increased.

Muscle spasm and tenderness on palpation over the pylorus, otherwise negative.

Dr. Friedenwald had the patient under observation for some time and examined the stomach contents repeatedly. There was marked hyperacidity. On March 19, the abdomen was opened in the usual way and a number of adhesions were found about the pylorus, which was fairly movable. After freeing the adhesions, this operation was carried out

very satisfactorily. The patient, although not in very good condition at the time, stood the operation very well, and made a rapid and complete recovery.

I saw her a few days ago; she had regained her forty pounds and was looking the picture of health. She said she ate anything and everything and digested it with no difficulty.

*Case III.*—Mary M., aged twenty-eight, entered the Johns Hopkins Hospital April 12, 1901, referred to me by Dr. J. Friedenwald, of Baltimore, complaining of "stomach trouble."

Family history negative, no tuberculosis or cancer. History of trouble dates back twelve years, during which time she has suffered always more or less after eating. No appetite. Very constipated. No history of injury.

Her chief complaint is distress after eating, occasional attacks of bloating of stomach and vomiting with pain. Epigastric distress increased by food, relieved by vomiting. Pain radiates to back and right side. Two years ago had severe hemorrhage. Vomitus occasionally suggests coffee grounds. Has lost thirty pounds in weight. Is very weak, and for the last two years has lived on milk, soup, and crackers. She has used the stomach tube for the past year daily.

Patient is very pale, thin, and anæmic looking. Heart and lungs normal. Abdomen not distended, slight tenderness over epigastrium.

Area of gastric tympany increased. Liver dullness normal. Palpation negative.

She had been in the Johns Hopkins Hospital two years previously when an exploratory laparotomy had been performed by Dr. Halsted.

The organs all seemed normal at that time, no thickening about the pylorus. A longitudinal incision was made in the anterior wall of the stomach near the pylorus through which the mucous membrane was examined and no lesion found. No apparent contraction of the pylorus. Stomach wound was closed, no drainage.

She was relieved of her symptoms for about one year. Eighteen months later she entered my service at the Union Protestant Infirmary. Her condition at that time was about the same as before the operation. I opened the abdomen expecting to do a gastroenterostomy. I found many adhesions about the pylorus and lower end of the stomach which doubled it in upon itself and decreased the lumen markedly. After these adhesions had all been separated, I invaginated the anterior wall of the stomach on my finger and passed it through the pylorus which seemed about the normal size. I could dilate it easily. The stomach not being noticeably enlarged, it seemed as if the development of adhesions after Dr. Halsted's operation had been responsible for the return of the trouble. I, therefore, having stretched the pylorus thoroughly with my finger, after the method of Hahn, closed the abdominal wound without drainage.

She was again relieved of her symptoms, but only for a few months, and reentered the Johns Hopkins Hospital on April 12, 1901, for a radical operation. Her condition at that time has been described. On opening the abdomen a great mass of adhesions was encountered, binding together the liver, stomach, duodenum, omentum, and parietal peritoneum. Considerable time was consumed in separating these adhesions during which hemorrhage was quite free but easily controlled by pressure and ligature. The pylorus was bound up in adhesions to the omentum, gall bladder, and liver. The left lobe of the liver was thinned and very adherent to the anterior surface of the stomach. The pylorus was quite indurated and thickened. The stomach was considerably dilated.

After freeing all the adhesions, the stomach and duodenum were brought together, and an anastomosis established between them in the manner described.

Notwithstanding the many and dense adhesions and the thickness of the walls of the pylorus, the operation, once the adhesions had been separated, was accomplished without further difficulty.

She made a good recovery and is now completely relieved of her trouble. I saw her a few days ago, and she had gained about forty pounds, and says she eats and digests anything she wishes.

*Case IV.*—J. M. B., referred to me by Dr. J. Friedenwald, of Baltimore; aged forty-eight, barkeeper; admitted to the Johns Hopkins Hospital March 18, 1902, with the history of "stomach trouble" for years, also that a piece of stomach tube had broken off in the stomach during the act of washing out.

Family history negative, no tuberculosis, no cancer. Patient has had the usual diseases of childhood, typhoid fever, pneumonia, very subject to cold, has had a cough, now, for four years. Has been a very hard drinker. The patient gives the history of having had indigestion and "stomach trouble" for twenty years. Began with pain and vomiting after eating. Has been very severe at times, radiating to back and right shoulder blade. Eighteen years ago had severe hemorrhage from stomach. He has had a great deal of trouble ever since this time, frequently vomiting food that has been in his stomach for several days. He has been under treatment during most of the time, having consulted many physicians. Bowels irregular.

About three years ago, by the advice of his physician, he began the use of the stomach tube, but discontinued it after a time. Eleven days ago, while using an old tube, that he had had for five years, it broke and more than half of it remained in the stomach. The patient insists, that during the time this piece of tube has remained in his stomach, he has been feeling better than for years past.

Examination of the patient shows an extremely pale and emaciated man. In the chest there are indications at both apices of beginning tubercular trouble. Heart negative. Abdomen rather full, considering the extreme emaciation; liver dullness about normal. Stomach tympany extends over 1 cm. below the umbilicus, and well beyond the middle line.

Palpation of the abdomen negative. No movable dullness detected. Marked œdema of both legs. Finger nails markedly clubbed.

On March 19, abdomen was opened under Schleich's solution anesthesia, after preliminary hypodermic injections at hour intervals, of one-sixth of a grain each of morphia, hypodermically. There was considerable ascitic fluid in the peritoneal cavity.

The stomach was found to be much enlarged and displaced downward. Liver about normal in size, rather hard, with some scar tissue over the pylorus. Gall bladder slightly distended but not adherent. The pylorus was very much scarred and puckered. Its walls much thickened and indurated. It was very adherent to the liver and transverse colon.

The omentum was tightly bound to it in several places. The pylorus itself was so firmly fixed by the adhesions from below, that it was possible to raise it but slightly. The duodenum was adherent near the pylorus but free below. It was found possible to oppose the stomach and duodenum after freeing the adhesions about the pylorus. The operation of pyloroplasty was then performed in the way already described. It differed only in that the incision was made considerably longer, about 15 cm. in length. The dense scar tissue in the anterior wall of the pylorus, and the neighboring portion of the stomach was excised. The wall of the stomach at this point was very dense and firm and over 1 cm. in thickness. A portion of stomach tube about 35 cm. long was found in the stomach and removed.

There was no difficulty in applying the sutures, and the operation was carried out with great facility. The whole procedure occupied about fifty minutes.

The patient stood the operation well, and up to the present time (3 months) has been doing uninterruptedly well.

*Case V.*—J. A. W., aged twenty-two, referred to me by Dr. L. P. Hamburger, of Baltimore; a farmer by occupation; admitted to the Union Protestant Infirmary May 23, 1902.

Complains of burning and a sense of weight in the stomach. Several paternal aunts were afflicted with consumption. No history of tumor. Does not use alcohol or tobacco.

Present illness began three and a half years ago with la grippe. Following this illness, he was left weak. During the summer of 1898, he belched much and regurgitated his food. Up to November of 1898, lost about ten pounds. At this period, he gave up work because of weakness and a "pulling" sensation in the abdomen. The winter of 1898-99, he spent in the Maryland General Hospital and has gone the rounds of hospitals and doctors ever since, without improvement. In the spring of 1898 weighed one hundred and forty pounds, and in the spring of 1899 weighed one hundred and five pounds. Because of the burning sensation in the abdomen, he has been obliged to limit his diet since 1899 to eggs, milk, cocoa, and toast. Complaint has continued off and on in varying intensity ever since. In addition, he is compelled to expectorate saliva almost continually. Has never vomited blood.

He is worse in the summer, and there is a slight improvement in the winter. His average weight now is one hundred and twenty-seven pounds. His appetite is good, but any increase in his diet causes diarrhea.

On physical examination, patient is very poorly nourished, tongue lightly furred, mucous membranes fairly good color. Patient blushes readily.

Heart and lungs clear. Temperature 99°. Abdomen looks natural. Distinct clapotage in the left hypochondrium. The right kidney is distinctly palpable. Outline of stomach tympany on inflation from left nipple to 3 cm. below umbilicus.

An Ewald test meal showed free hydrochloric acid, no lactic acid.

On May 30, 1902, I performed the operation of pyloroplasty by the method described. On opening the abdomen, the stomach was found to be slightly dilated and its walls quite flabby. At the pylorus, on the anterior wall, was the puckered scar of an old ulcer. The pylorus would not admit the tip of the index finger. Posteriorly, there were some adhesions between the stomach and duodenum. When these had been thoroughly freed and the scar tissue in the anterior wall of the stomach had been excised, the operation as described was performed.

The appendix was found very long and bound down by adhesions on the anterior surface of the ascending colon. As the tip of the appendix was adherent to the gall bladder, the appendix was excised.

The patient has made an excellent recovery and at the present time, one month after the operation, has gained several pounds. He is eating and digesting regular hospital diet, and expresses himself as very much relieved.

From my study of the other methods suggested for the relief of benign stricture of the pylorus, and from my experience in the foregoing cases, I believe the following conclusions are justified:

(1) All the operations heretofore suggested for the relief of benign stricture of the pylorus are open to serious individual objections.

(2) The operative procedure made use of in the cases here reported combines more good points and less objectionable features than any other method that has been suggested up to the present time.

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FIG. 1.

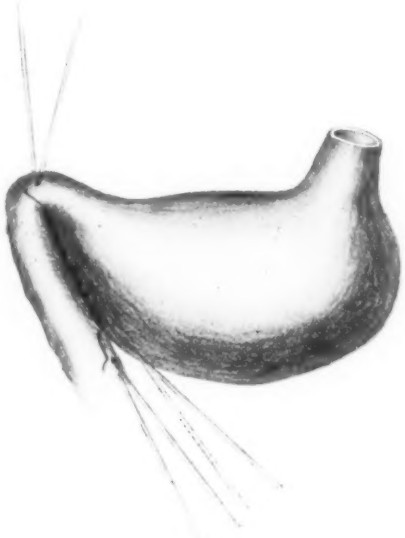

FIG. 2.

FIG. 3.

FIG. 4.

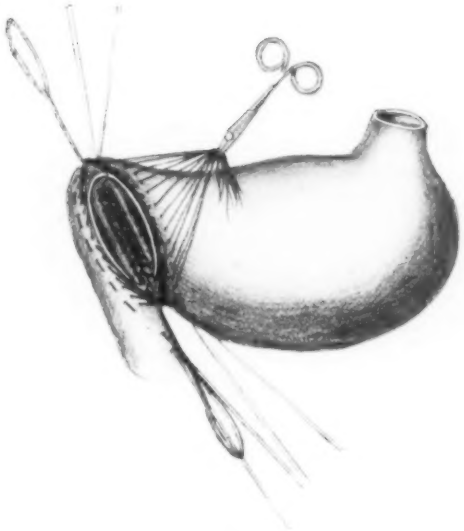

FIG. 5.

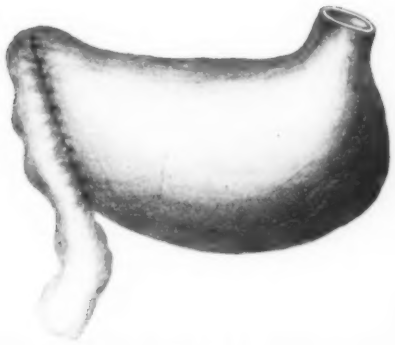

FIG. 6.

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# THE SURGICAL TREATMENT OF TUBERCULOUS CERVICAL ADENITIS.

BY JAMES F. MITCHELL, M. D.,
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This communication is based on the study of 170 cases of tuberculous disease of the lymphatic glands of the neck, treated in the service of Dr. Halsted in the Johns Hopkins Hospital between August, 1889, and February, 1902.

An effort has been made to examine the patients personally, or to communicate with them or their physicians by letter. Owing to the frequency of the affection in the colored race and in the lower classes in general, individuals whose residence is constantly changing, the cases have proved unusually difficult to follow and a very large number have to be recorded as lost.

Especial attention has been paid to the complications and remote affections after the operation and to the condition of the lungs, and a comparison made between our findings and the statistics given in recent literature. Articles by Blos, Jordan, and others have been freely drawn upon, although no attempt has been made to review the enormous literature of this subject. Many of the earlier histories are incomplete in details, especially in the examination of the lungs. Of the 170 cases, 27, for various reasons, did not receive truly surgical treatment, or the records were too incomplete to be of service. These will, therefore, not be considered in discussing the results, thus leaving 143 upon which our statements are based.

*Frequency.—Race, Sex, Age.*—Of 13,000 surgical patients, 1098 were admitted for tuberculosis, and of these, 170 with tuberculous glands of the neck; that is, 8% of all the surgical patients were admitted for tuberculosis, and 1.3% of all for tuberculous glands of the neck. The neck cases comprise 15% of all those with tuberculosis, and are exceeded in number only by those with hip-joint disease. Of whites there were 83 cases; of negroes 61, that is about 4 to 3. The average ratio of whites to negroes in the hospital is 7 to 1, so that it is evident that the disease is more prevalent among the negroes. Like all tuberculous affections, it is found where hygienic conditions are poorest, 82% living in the city, 18% coming from the country or small towns. Males outnumber females as 3 to 2. The youngest was 18 months, the oldest 66 years of age. The average age is somewhat younger in females. Between 10 and 30 there occur 76%. This corresponds exactly to the statistics of Fuernrohr in Erlangen. Tabulation according to decades gives the following:

| Age.... | 1–10 | 10–20 | 20–30 | 30–40 | 40–50 | 50–70 |
|---|---|---|---|---|---|---|
| Cases.. | 16 | 36 | 54 | 8 | 7 | 2 |

These ages are taken at the time of admission for treatment and, according to Blos, do not represent the true beginning of the disease, but rather the time at which a latent infection begins to develop, that is about and after puberty. Volland noted that in the Swiss schools 96.6% of children between 7 and 9 years of age had enlarged cervical glands; this high percentage gradually decreasing until puberty. To this condition the term scrofula, if used at all, should be restricted; that is, a chronic hyperplasia, gradually decreasing as puberty is approached. Such swollen glands offer conditions most favorable to tuberculous infection, and it is possible that the infection may take place at this time, and remain latent until after puberty.

*Duration.*—The duration of the disease before admission, as noted by the patients, varied from 1 week to 20 years in our cases.

| Months.. | 0–2 | 2–4 | 4–6 | 6–8 | 8–10 | 10–12 | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Years.... | | | | | | | 1–5 | 5–10 | 10–15 | 15–20 | 20– |
| Cases.... | 9 | 13 | 10 | 14 | 3 | 4 | 52 | 13 | 2 | 2 | 1 |

Many give a history of fluctuation in the size of the glands, and in some the swelling has at times entirely subsided to reappear in the course of months or years.

*Etiology, Infection, Heredity.*—As to the source of infection our histories show little; apparently this point was not well considered in the examination of the patients. Four followed la grippe, three diphtheria, one coryza, bronchitis, or catarrh, and one was attributed to a blow in the neck, while one followed pediculosis capitis. About one-half give a family history of tuberculosis. This is much larger than the proportion given by Blos, 28% in 851 cases. It is ordinarily stated that one-third give an hereditary history. The disease was formerly thought to be a local manifestation of a general infection. The opinion at the present time is that

it is as a rule primarily local. The infection is evidently a descending one and various parts of the pharynx are assigned as portals of entry, of which the tonsil is the most common, an hypertrophied tonsil especially offering favorable conditions for infection. There is not necessarily a tuberculous lesion at the point of entrance. Nicoll has found tubercle bacilli in tonsils and adenoids when there was no tuberculous lesion here or elsewhere. Carious teeth may also be a starting point, and Stark has demonstrated tubercle bacilli about their roots. The disease sometimes follows acute exanthemata and some cases can be attributed to diseases of the skin about the face or head. Cervical glands comprise about 90% of all tuberculous glands. This is probably explained by the fact that the glands of the neck, owing to the area which they drain, are especially subject to inflammatory swelling in childhood, and such hyperplastic glands offer favorable ground for tuberculous infection.

*Glandular Involvement.*—The distribution of the glands affected speaks strongly in favor of a descending infection, 70% being in the superior triangle, and where all the triangles are involved, the disease is generally more extensive in the upper portion of the neck. The glands of the neck may be roughly divided into four groups; those in the anterior triangle and those in the posterior, with two connecting chains, one passing in front, the other behind, the sternomastoid muscle. The connecting chain behind the muscle seems to be the one most commonly involved, a fact which accounts for much of the difficulty of operation. The right and left sides of the neck are affected with about the same frequency, and fully one-half the cases have involvement of both sides. The axilla is often secondarily involved, seven times in our list. Axillary infections are probably always secondary to infection of the neck, unless there is some definite tuberculous lesion, as of the ribs or fingers, in the region which these glands drain. In only two cases was there also involvement of the glands of the groin or the popliteal space. One case had been operated upon previously for tuberculous peritonitis, one for lumbar abscess, and one had a previous history of tubercular meningitis, one of tuberculosis of the dorsal vertebræ, one of tuberculosis of the knee.

*Condition of the Lungs.*—In 34 cases there was no note on the condition of the lungs before operation; 89 were stated as being negative; 13 as suspicious, and 7 showed positive evidence of tuberculosis. Taking together those cases in which the lungs were definitely tuberculous or in which there was a suspicion of tuberculous infection, there are 14%. while only 4.9% showed positive evidence of tuberculosis. In various statistics these percentages differ widely, thus Fraenkel states that lung involvement is present in about 10.2%, while Jordan had 26%. An average of five different statistics would show about 19% of cases with affection of the lungs. According to Blos, tuberculosis of the glands of the neck serves as a frequent source of infection for the lungs, the course of the infection being either through the lymphatics or the blood.

*Pathology.*—The glands differ widely in their appearance and in the same neck may show all degrees of involvement. According to Jordan, they may be divided into four groups, all of which are stages of the same process, and all of which may be found existing together. The simplest of these forms is pure hyperplasia. Here there is a general enlargement of the glands of the neck without the formation of any nodes, the glands on section showing a homogeneous structure and their true nature being disclosed only by the demonstration of tubercle bacilli. There is nothing macroscopically or microscopically pathognomonic. The bacilli are very few in number and their presence can often be demonstrated only by animal inoculation.

The second type is characterized by the formation of nodes. On section one sees scattered over a gray or grayish-red background fine lighter grayish points, which under the microscope are shown to be typical tubercles. The size of the nodes varies from that of a pea to an egg, all presenting on section the same appearance.

The third type is characterized by caseation. The tubercles have increased in number and the gland has undergone retrograde metamorphoses. The whole gland may be converted into a caseous mass and even the smallest ones may show the same structure. The gland may be entirely broken down and converted into an abscess bounded by its capsule.

In the fourth group the inflammation has spread to the periphery and involved the gland capsule and the periglandular structures. There is new formation of connective tissue, binding together neighboring glands and surrounding structures, skin, muscle, etc. The glands may have completely broken down and coalesced to form a large cyst filled with pus and caseous matter. In one case we had such a cyst extending from the mastoid process to the spine of the scapula 7 cm. below the clavicle. The skin may become involved and eventually the abscess burst and ulcers and discharging fistulæ result. These forms may be all combined, and in addition there may be a pyogenic infection which can lead by abscess formation to actual cure of the tuberculous process in any stage. There may also be a calcareous deposit, or a tuberculous process may be encapsulated in connective tissue and remain quiescent or subject to exacerbations.

*Symptoms.*—The clinical picture is usually a characteristic one. The patient, ordinarily a young person, presents himself with a tumor of varying size, situated, or at any rate most prominent, in the upper part of the neck, with perhaps scars of old abscesses or possibly the presence of ulcers and fistulæ. There may be slight fever, although as a rule it is absent. Pain also is usually wanting, although sometimes, if the tumor is large, there may be pain from pressure on the cervical nerves. There is often slight anæmia, the hæmoglobin varying from 70% to 80%. There may be some loss of weight.

*Diagnosis.*—The diagnosis is generally easy. At times it may be difficult to distinguish from actinomycosis, syphilis, lymphosarcoma, Hodgkin's disease, carcinoma, cysts, or

chronic hyperplasia. Most of these affections can be ruled out by the character of the tumor or the presence of other manifestations of disease. The removal and microscopical examination of a gland will generally settle the question if there is any doubt. Too much emphasis cannot be laid on the tuberculin test. We have records of 25 cases in which tuberculin has been given to patients suffering from tuberculous cervical adenitis, and one in which Koch's lymph was given. In this last case the patient was reported discharged well four weeks after the last injection and there is no further note, the patient being subsequently lost sight of. This case is interesting inasmuch as general tuberculosis followed in two cases of tuberculous arthritis in which Koch's lymph was given. The tuberculin used was made by Dr. Trudeau, and reaction followed in all but one of the 25 cases. In this case a note on the history states that the same sample of tuberculin gave no reaction in several other cases which were known to be tuberculous. It may possibly be explained by the dose being too small, or there being some error in its administration. As tubercle bacilli had been demonstrated in the sputum, it was undoubtedly a case of tuberculosis. In all of the cases but one in which there was a reaction there was evidence of tuberculous disease found at operation. This patient was discharged not treated after a positive tuberculin reaction. Twenty of the 25 patients reacted to the first injection. The average time before the temperature rose was about 8 hours; the duration of the reaction following about 30 hours. The temperature ranged somewhat higher than is common in tuberculosis of other organs of the body. In 9 cases it was above 102°; in one case it reached 105.5°. General symptoms, such as headache, loss of appetite and general discomfort, were common. Local symptoms were observed in comparatively few cases. In a number of cases in which it was difficult to say whether the patient was suffering from some form of cyst or from tuberculosis, and in all cases of Hodgkin's disease, tuberculin was given. There was no reaction in any but tuberculous cases, and in no case have we seen any ill effects from its administration.

*Prognosis.*—The outlook depends upon the form, stage, etc., of the disease and on the complications, especially tuberculosis of the lungs. Tuberculous gland disease is seldom in itself fatal. The prognosis is worse in children, and improves with age. It is worse where there is a history of heredity, and the outlook is necessarily more grave where there have been recurrences. Tuberculosis of the neck in general is one of the forms of tuberculosis which remains longest local. Spontaneous healing is possible in all stages by encapsulation or by the formation and rupture of an abscess, as is strikingly demonstrated by the large number of persons one meets on the street, with ugly contracting or keloidal scars in the neck. This, however, should not be counted upon; and the tuberculous focus is always a danger to the organism as a point from which tuberculosis may spread. In 16 of 308 cases of Blos there was spontaneous cure without any interference.

*Treatment.*—Treatment may be constitutional, by local applications, or by operative procedure.

*Constitutional treatment* consists in attention to hygienic surroundings and improvement of the general condition by life in the open air, sea bathing, or the administration of tonics, cod liver oil, creosote, etc.; and whether local applications or operative procedures are resorted to, constitutional treatment should be recommended both before and after. In a recent report from Guy's Hospital, Dr. Harnett emphasizes the importance of hygienic measures and thinks that operative procedures are too often resorted to and are much too extensive. If the glands have not become very large and are not broken down and have existed for less than two years, hygienic measures, he thinks, should be first tried, and provided these are carried out and continued for long periods there is no doubt that in a large proportion resolution will occur. If, on the other hand, the disease has existed for over two years and the glands have attained considerable size, he advises the removal of the enlarged glands by enucleation through numerous transverse incisions. He bases his remarks on 200 cases, although his results are not stated. Undoubtedly many cases, especially those in the stage of simple hyperplasia, will entirely subside under constitutional treatment alone.

*Local treatment* consists in the application or injection of various substances, as iodine. Of our cases 28, afterwards operated upon, had been previously treated by the application of iodine locally, or by injections of iodine or iodoform, sometimes combined with incision, or by the rubbing in of various ointments. This latter practice cannot be too strongly condemned as it can only serve to encourage inflammation about the glands, and we have never seen any permanent good results from local treatment in any form.

*Operative procedure* may be conservative or radical.

*Conservative treatment* consists of simple incision and curettement with the application of iodoform, or of partial excision of the glands, that is removal of those glands which are seen to be definitely tuberculous. Simple incision is to be recommended only as a measure preliminary to the later radical operation, although many cases have gotten well with no other treatment. Twelve cases have been so treated, in all of which iodoform was applied at the time of operation. Where a single gland is involved, which is most common in the submaxillary region, results from this procedure have been very satisfactory, iodoform apparently having a certain retarding effect on the tuberculous process. Partial excision, or removal of the involved glands only, has been resorted to in 69 cases.

*Radical operation*, that is removal of all the glands with the surrounding fat, has been done in 59 cases. The operation of complete excision of the glands of the neck may be extremely difficult, especially where there is sinus formation or suppuration with extensive periglandular adhesions. The selection of an incision admits of much choice and numerous

methods have been recommended with a view to getting the best exposure with the least resulting scar. The operation as usually done in this hospital is as follows: A long incision is made beginning behind the ear over the mastoid process, curving forward over the edge of the sternomastoid muscle, and then slightly backward to the middle of the clavicle. A transverse incision is then made along the clavicle, forming a T. The skin is now dissected back, giving a large quadrilateral exposure, through which all parts of the neck can be easily reached, even the submental region. The dissection is now begun in the angle between the posterior border of the sternomastoid muscle and the clavicle. The subcutaneous fascia and platysma muscle are divided and turned back and a few posterior fibres of the sternomastoid severed, thus exposing first the external jugular vein. This is divided and ligated and brings one directly to the omohyoid muscle, which serves as a key to the operation. The omohyoid is seized with two clamps and cut, and becomes an excellent retractor and guide. By following it the internal jugular vein is readily exposed in spite of any amount of adhesions. Using the omohyoid as a retractor, the sternomastoid is pulled aside and the dissection carried up along the internal jugular vein and the posterior border of the sternomastoid until the posterior branch of the spinal accessory nerve is encountered. This is dissected out of the mass of glands, and the glands delivered beneath it. The whole dissection is thus carried from below and from the middle line upwards and outwards. By following these steps the operation is greatly simplified and a great advantage is that the internal jugular vein is exposed in its lowest portion at the very beginning of the operation. A provisional ligature can be passed around it and if the vein is later injured above, the entrance of air is readily prevented. The most difficult stage of the operation is reached in the upper part of the neck. The chain of glands which is always involved, and usually most extensively involved, is that group connecting the anterior and posterior triangles behind the sternomastoid muscle. Through the midst of these glands the spinal accessory nerve passes and it is often so intimately adherent to the mass of glands that its separation involves most difficult dissection. The greatest care should be exercised in leaving this nerve uninjured, as from it comes the supply to the sternocleidomastoid and trapezius muscles. These glands being freed, are delivered beneath the spinal accessory nerve and sternomastoid muscle, and with the glands from the lower portion of the neck are dissected upwards and outwards from the underlying structures. It is impossible in this dissection to avoid the cervical plexus and many branches of these nerves are divided. In mild cases many of them can be saved. The descendens noni can usually be saved and division of the vagus or phrenic is never necessary. When there is involvement of the sternomastoid muscle, removal of a portion or all of the muscle is indicated, and at times a portion of the trapezius also. If there is extensive periglandular inflammation and if the tuberculous process has spread beyond the glands and periglandular fat, it is sometimes impossible to save the spinal accessory nerve and the operation is made much less difficult and its duration shortened by hours by the following procedure: Following the omohyoid muscle as a guide, the sternomastoid is divided immediately after division of the omohyoid by using the omohyoid as a retractor and cutting across the sternomastoid low down in the neck on top of the omohyoid. In this way there is no danger of injuring the vessels and the division of the sternomastoid can be easily accomplished. The omohyoid passes beneath the sternomastoid below that point where the posterior branch of the spinal accessory nerve leaves the muscle, and this posterior branch having been freed, it may practically always be saved even after division of the muscle. The operation in these cases proceeds as follows: Having divided the omohyoid and the sternomastoid, the sternomastoid is reflected in both directions, exposing the whole of the region lying beneath it and leaving the anterior and posterior glands connected by the mass of glands lying beneath the sternomastoid muscle close against the mastoid process. It is possible and comparatively easy with this exposure to still preserve the spinal accessory in its upper portion, that is the portion supplying the sternomastoid muscle, although a sacrifice of the posterior branch may in rare cases be necessary. In all of our recent cases we have been able to save the nerve in both branches after division of the muscle. The internal jugular vein if involved in the process should be ligated and removed. This involves no difficulty and is followed by no ill effects and is advised in all cases by Watson Cheyne and others if the freeing of the vein is very difficult and there is danger of much hæmorrhage from its branches. The glands and surrounding fat having been thoroughly removed, the sternomastoid and omohyoid muscles are sutured with catgut. The skin is then closed with subcutaneous silver sutures and a rubber protective drain is placed through a buttonhole in the outer flap of skin, which is the most dependent part of the wound for the first twenty-four hours. This drain never causes any trouble and is removed at the first dressing at the end of a week or ten days. It is a great safeguard and prevents that filling of the wound with serum which is so apt to occur and which may prevent primary healing. The neck is fixed by a large dressing of gauze and plaster of Paris, reinforced by thin basswood splints and embracing the head and shoulders. The patients are allowed to sit up on the day following the operation and to walk about the ward within twenty-four hours. The division of the sternomastoid muscle and the spinal accessory nerve is to be most carefully avoided whenever possible; but in very adherent cases, if there is sinus formation, it is impossible to thoroughly remove the glands without dividing the muscle and possibly injuring the nerve, and the resulting deformity is so slight that it is not noticed by the patient unless his attention is called to it. The advantages of free exposure are only to be appreciated after operating upon a number

of adherent cases. The resulting scar is in most cases slight, although it shows above the collar and, being in the perpendicular direction, is more apt to spread than are transverse incisions. The incision used here is much the same as that used by Watson Cheyne. Harnett, with a view to avoiding the spreading of a perpendicular scar, advises several transverse incisions with the removal through each, of those glands which can be reached, but it hard to believe that a thorough removal can be done through such incisions. The incision recommended by Dowd, and previously by Baetson of Glasgow, begins in the anterior triangle beneath the jaw, runs back just beyond the hair line, down within the hair line to the lower portion of the neck, and then forward along the clavicle, turning forward a large skin flap. It has the advantage of leaving the perpendicular portion of the scar to be covered with hair and the transverse portions hidden above in the fold of the neck beneath the jaw and below by the collar. Whatever incision is used, however, the first object should be to obtain a free exposure of the whole side of the neck, and in severe cases where there is sinus formation the incision has to be modified according to the location of sinuses. While cosmetic considerations should always be borne in mind, complete removal of the glands is the first point to be thought of, and the incision should be made with a view to this rather than with fear of the resulting scar. One can always count upon the glandular involvement being much more extensive than it appears from external examination and the incision should be made with this in mind. A case in which the glands appear externally as a small mass in the upper part of the neck is apt to show at operation a chain of involved glands along the internal jugular vein which may extend all the way to the clavicle. The above incision has been found most satisfactory in 60 cases of tuberculous cervical adenitis operated upon by the writer in the last three years and in many cases of Hodgkin's disease or carcinoma or sarcoma of the cervical glands.

*Complications and Immediate Results.*—The dangers of the operation are slight and its mortality practically zero. In the 328 cases reported by Blos in Heidelberg there were no deaths, although the operations were done for the most part by younger assistants. In 10 statistics collected by him there were only three in which there was death from operation. Occasionally we have seen tacchycardia for a few days. Shock is extremely rare. There is little hæmorrhage after the skin is reflected and if the internal jugular vein is exposed in its lower part early in the operation, there is no danger from its injury, as hæmorrhage from it can be easily controlled by pressure with the finger until the vessel is secured. In early cases in which this precaution was not observed there were twice alarming symptoms from entrance of air, the patients becoming cyanosed, with rapid respirations, and the pulse rapid and intermittent. In both of these, however, the symptoms soon passed off. The internal jugular vein has been many times removed, and in a few cases the carotid artery also, with no ill effects.

On the left side of the neck the *thoracic duct* must be considered, extending as it does often a couple of centimetres above the clavicle. Injury of the duct, however, does not seem to be the serious matter it was formerly thought. The duct has been injured four times in our series of cases. In the first of these the wound was a longitudinal tear. An attempt was made to suture it and a drain was placed leading to the duct. The suture, however, was unsuccessful and there was leakage from the duct for two weeks, during which the patient lost 13 pounds in weight. The leakage was then controlled by packing with absorbent cotton and the patient rapidly recovered. In the second case the duct was cut directly across, being adherent to involved glands. It was about 3 mm. in diameter and its suture was difficult. The distal end could be seen to dilate with respiration and to eject chyle. The proximal end was collapsed. The posterior portion was held in position by connective tissue surrounding the duct. We were able to do an end-to-end suture by means of very fine curved needles threaded with silk fibre. On completion of the suture, the duct on both sides of it could be seen to distend with respiration and there was evidently free circulation within it. The suture held and there was no leakage after operation, although the wound suppurated, the patient having previously had a streptococcus infection of a sinus. This is the first case of end-to-end suture of the thoracic duct we find recorded. In the third case the duct was nicked and a lateral ligature applied. There was no leakage afterwards. In the fourth case, in separating some very adherent glands in the lower angle of the left side of the neck, the duct was so torn that its ends could not be brought together. It was ligated and no ill effects resulted. It would seem from these cases that leakage from the duct after operation is the thing to be avoided and if possible an immediate suture done.

Allen and Briggs recently report 17 cases of traumatic injury of the thoracic duct in the neck, including those reported by Cushing and others, and suggest that as a preventive measure the patient should be given a quantity of cream a few hours before operation, thus enabling one to more readily recognize the thoracic duct. As to treatment, they recommend packing rather than ligation as offering the best chances for the establishment of collateral circulation. In a very difficult operation for Hodgkin's disease recently done by Dr. Halsted, the duct was cut across close to its entrance into the vein in such a way that the cut ends were separated by a distance of a centimetre, and it was impossible to bring them together. The central end could be seen standing wide open and empty. The duct was ligated both centrally and distally. The patient recovered and showed no bad results.

The *paralyses* resulting from the operation are usually slight. In cases where the parotid lymphatics are involved, a careful dissection must be made to avoid injuring the facial nerve. Occasionally one of the lower branches of this nerve is injured and a slight paralysis of the lower lip results.

This has always proved temporary. There has been temporary injury of the hypoglossal nerve in one or two cases. Paralysis of the sternomastoid and trapezius muscles produces a deformity which is visible. As a rule, patients do not notice it, although, of course, it is to be avoided when possible. There may be slight drooping of the shoulder from paralysis of the trapezius and a sinking in of the neck from atrophy of the sternomastoid. The omohyoid often regains its function after suture, its nerve supply, the descendens noni, being commonly uninjured. The functions of the sternomastoid are assumed by the deeper muscles of the neck, and in no case has there been observed any limitation of motion due to its atrophy or even its complete removal. In a case of carcinoma of the cervical glands we once removed both sternomastoid muscles and there was little if any resulting limitation of motion. The sensory disturbances vary a great deal. In some cases there is practically no loss of sensation in the skin after a short time. In others there is a wide area extending over part of the ear, the neck, shoulder and arm, over which there are marked changes in sensation to touch, temperature and pain but these changes are usually unnoticed by the patient until his attention is called to them. It seems possible that by exposing the cervical plexus as it emerges behind the sternomastoid muscle and cocainizing it that the whole operation might be done with cocaine anæsthesia but this has never been attempted. Occasionally patients speak of a feeling of numbness to which they soon become accustomed. Rarely there are small areas of hyperæsthesia in the skin of the neck. The incisions as a rule heal per primam, although in cases where there has been sinus formation with secondary infection, suppuration may take place.

*Late Results.*—In considering the late results of the operation, a much smaller number of cases can be considered. Fifty-three cases have been absolutely lost sight of, while 22 have not responded to letters; 10 occurring in the last year are much too recent to consider, leaving 58 for examination. Of these, 45 or 77.6% are well with no local or other recurrence, and with negative lungs after periods ranging from 1 to 13 years.

| Years... | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cases... | 6 | 11 | 3 | 3 | 2 | 2 | 6 | 4 | 4 | 0 | 12 | 2 | 1 |

Of these cases, 24 had had more or less incomplete excision of the glands, 3 had been treated by simple incision and curettement, and 18 by complete excision. It is therefore shown that many cases undoubtedly recover without complete excision, although it is evident, from a consideration of the recurrent cases, that recurrences are much more common after incomplete removal of the glands. The small number of well cases that have had the radical operation is due to the fact that the extensive operation has been a gradual development from simpler measures and was not used in the earlier cases. Of 328 cases reported by Jordan and Blos, 140 were followed; 73% of all these were well. Eighty-two cases were observed after six years and of these 52.4% were well with no recurrence; 30% had local recurrences. Eleven statistics, comprising in all 745 cases, show 54% well, 28% with recurrence, and 18% dead. Our results thus compare very favorably with statistics elsewhere, showing 77.6% well, 15.5% dead, and 6.9% living with recurrence. In 21 cases (15%) of the 143 there have been recurrences. In 2 of these the recurrence was on the opposite side. In 2 it was evident at the operation that the removal was not complete and the recurrence dates from the operation. In 4 cases after complete operation there was recurrence at the seat of operation. All other recurrences followed incomplete removal of the glands, or simple incision and curettement. All of the recurrences were within a year; the average time of recurrence being about four months. Many of the recurrent cases were subsequently operated upon. Of the ultimate results, 5 were lost, 2 were not heard from, 1 is dead of general tuberculosis, 1 developed tuberculosis of the lungs fourteen months later and was subsequently lost, 4 are living with recurrences, and 8 are well. Therefore, about 38% of those cases which recurred after a first operation, complete or incomplete, have remained well after subsequent operations. As previously stated, the condition of the lungs before operation was noted as suspicious of tuberculous involvement in 13 cases and as definitely tuberculous in 7 cases. In Jordan's cases 26% showed involvement of the lung before operation. Of the 13 suspicious cases, 6 have been lost track of, while 2 have not responded to letters. Of the remaining 5 cases, 2 are well with negative lungs and 3 are dead, one of tuberculous peritonitis two years after operation, the other 2 from causes not tuberculous, 4 years after operation. Of the 7 showing positive evidence of tuberculosis of the lungs, 2 are lost, one is well two years after operation, one has general tuberculosis, while 2 have died with tuberculosis of the lungs, and one with general tuberculosis. Only one case with definite tuberculosis of the lungs before operation is, therefore, known to have recovered. There are records of 3 cases in which operation was not advised and the patients were not treated because of tuberculosis of the lungs. The experience of Jordan is much more encouraging. Of 140 cases, 20 had lung involvement before operation. At a later examination 16 of these were well and also free from glandular disease, and he concludes that the removal of the glands has a distinct curative effect in 80% of the cases. On the other hand, only one of our cases is known to have developed tuberculosis of the lungs after operation where the lungs were negative before operation, while 13 of 140 of Jordan's cases developed lung complications after operation. Unfortunately, our one case has been lost, the only note on the history being that the patient presented himself 14 months after operation with tuberculosis of the lungs. There have been 9 deaths in the 58 cases followed (15.5%). Two of these died of heart disease, one four years, one six years after operation; one of an acute non-tuberculous illness one year after operation; one from unknown cause 4 years after operation; one of tuberculosis of the lungs a year after operation; one of tuberculous peritonitis two years after operation, and three with

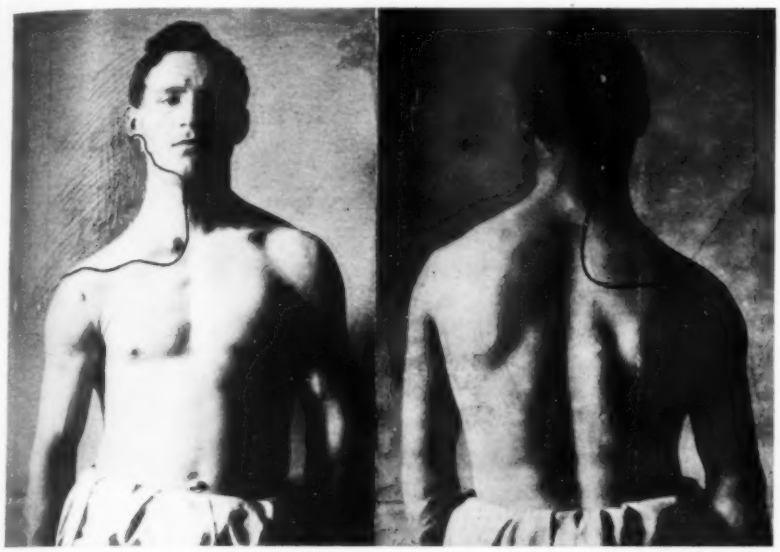

FIG. 6.—Marked droop of shoulder due to division of posterior branch of spinal accessory nerve. Area of anæsthesia following complete excision of glands of right side of neck.

FIG. 7.—Area of anæsthesia 2 years after excision of glands of neck with removal of sternomastoid and omohyoid muscles, internal jugular vein and common carotid artery.

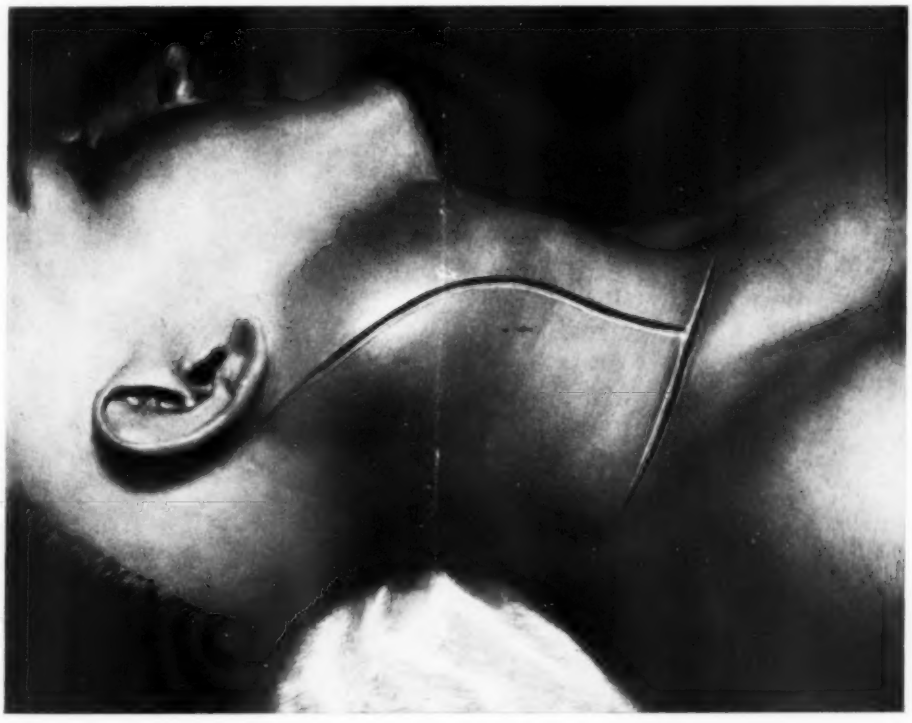

FIG. 8.—Skin incision for complete removal of glands of neck.

FIG. 1.—Characteristic tumor formed by tuberculous glands of neck.

FIG. 2.—Hodgkin's Disease forming large tumor in neck.

FIG. 3.—Keloidal scar and area of anæsthesia following complete excision of glands of neck.

FIG. 4.—Extensive anæsthesia following complete excision of glands of left side of neck.

FIG. 5.—Small area of anæsthesia where attention was paid to saving branches of cervical plexus in recent operation.

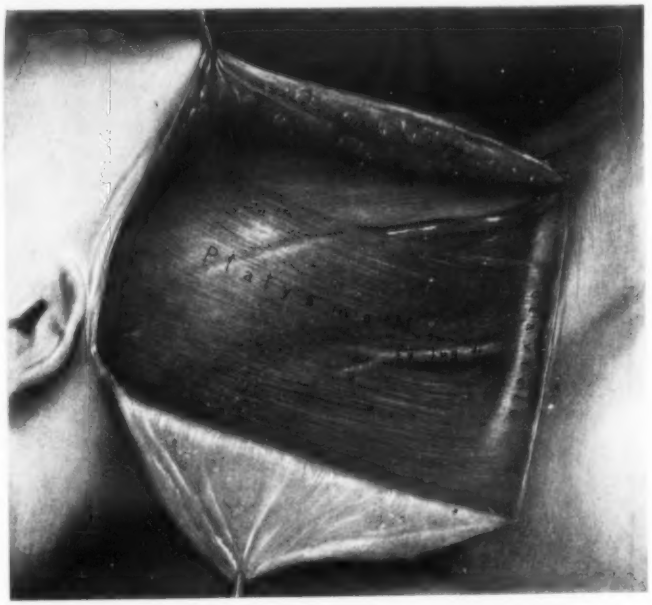

FIG. 9.—Skin flaps reflected showing quadrilateral exposure of all parts of the neck obtained through the T-shaped skin incision.

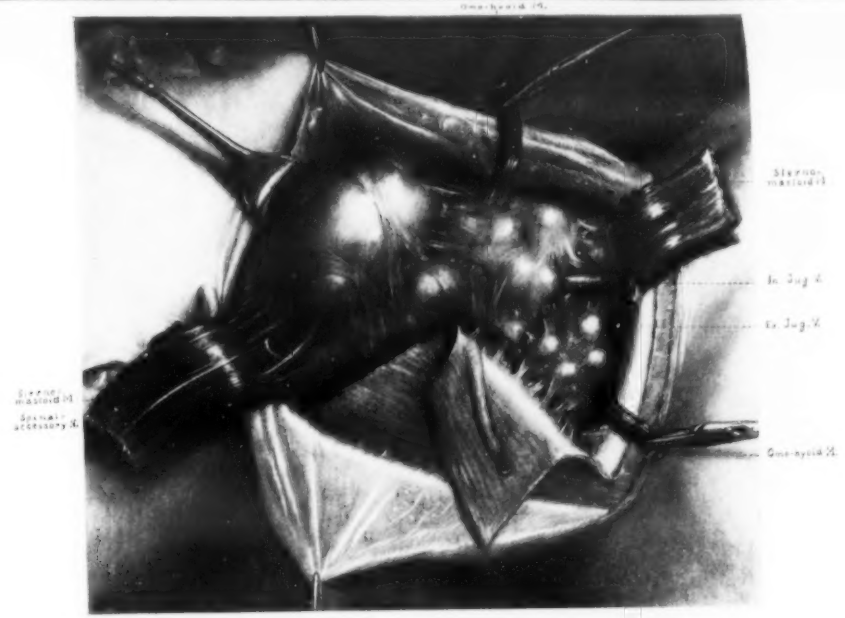


FIG. 10.—Omohyoid and sternomastoid muscles divided and reflected; external jugular vein ligated and divided.

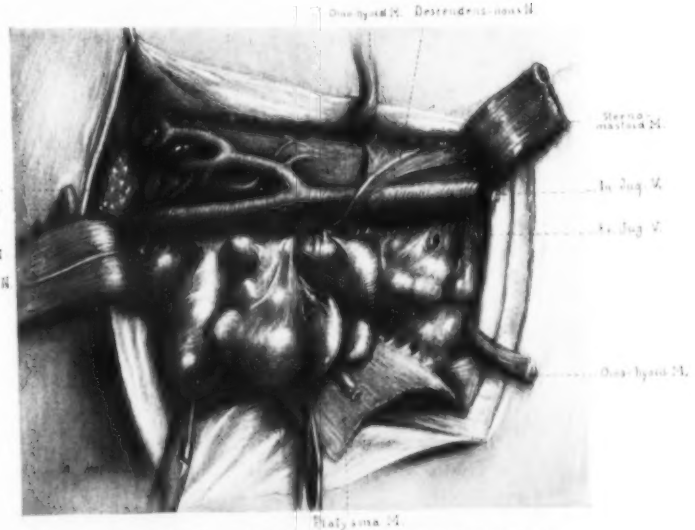


FIG. 11.—Glands dissected away from internal jugular vein.

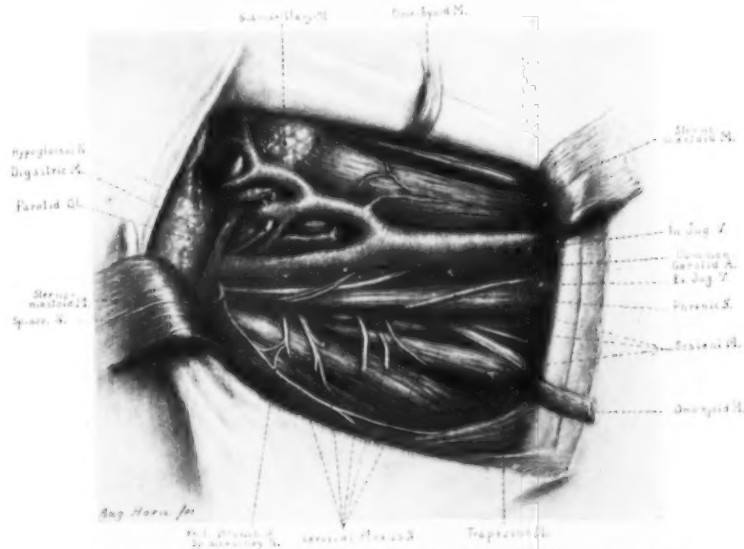


FIG. 12.—After complete removal of glands. Spinal accessory nerve intact, its posterior branch given off before entering sternomastoid muscle showing its anastomosis with cervical plexus.

general tuberculosis. Thus five cases have died of tuberculosis after operation. In the cases of Blos and Jordan there were 19% of deaths in 12 years. Eighteen of these were from tuberculosis. These statistics would indicate a much closer relation between tuberculosis of the glands of the neck and tuberculosis of the lungs than our cases show, and it is stated that about 28% of all usually die of tuberculosis elsewhere after operation. This corresponds very closely to the results in tuberculosis of the knee where it is stated that from 20% to 30% of all cases prove fatal from tuberculous affections. Unless there is general dissemination of the disease tuberculosis in other regions than the lungs is extremely rare after operation. One of our cases developed tuberculosis of both thumbs and is now well after subsequent operations. One had Pott's disease and later died of general tuberculosis, and one died of what was, from the physician's description, apparently tuberculous peritonitis.

*Conclusions.*—From the study of our own cases and their subsequent observation, and from the results of others, the following conclusions can be readily drawn:

(1) Tuberculous cervical adenitis is primarily a local disease of very frequent occurrence, more often in young persons; in itself not extremely serious and rarely if ever proving fatal.

(2) It bears, however, a certain definite relation to tuberculosis of the lungs and serves as the starting point from which tuberculosis may spread.

(3) The tuberculin test as an aid to diagnosis is positive and harmless.

(4) While recovery may often take place under good hygienic conditions, surgical interference is clearly demanded in most cases.

(5) When surgical treatment is resorted to the operation should be radical in all cases.

(6) Recovery may be predicted in 70-80% of cases so treated. Tuberculosis of the lungs after complete removal of the glands is comparatively rare.

(7) Tuberculosis of the lungs unless far advanced is not a contraindication to operation, the removal of the glands apparently exerting a beneficial influence on the condition of the lungs.

LITERATURE.

No attempt has been made to review all the literature. Extensive bibliographies will be found under references 1, 2 and 3.

(1) Blos, Edwin: Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie, 1899, IV, p. 520.

(2) Jordan: Handbuch der praktischen Chirurgie. Bergmann, Bruns und Mikulicz, 1900, II, p. 84.

(3) Dowd, Charles N.: Annals of Surgery, 1899, XXIX, p. 559.

(4) Cheyne, W. Watson: British Medical Journal, 1899, No. 2033, p. 1659.

(5) Harnett, C. J.: Guy's Hospital Reports, 1901, Vol. LV, p. 55.

(6) Allen, Dudley P., and Briggs, C. E.: American Medicine, September 14 and 21, 1901.

# THE LEUCOCYTE COUNT IN THE SUMMER DIARRHŒAS OF CHILDREN.[1]

BY J. H. MASON KNOX, JR., PH. D., M. D., AND LOUIS M. WARFIELD, M. D.

(*From the Laboratory of The Thomas Wilson Sanitarium.*)

Perhaps no subject in medicine has been more thoroughly worked over during the last few years than that of the blood. The chemical constituents of this fluid have been subjected to as searching analysis as the present state of chemical knowledge will permit, and to the data thus obtained very much of great importance has been added in the physiological and pathological laboratories. The several proteid bodies in the blood have been studied and their relationship to the gases and mineral solids in large part determined. More accurate methods have been introduced to estimate other principals which are present in normal blood in small quantities but which are of pathological significance when in excess. Among these substances may be mentioned urea, uric acid, glucose, glycogen, ferments, fat and bile. More interest of late years has been given to acetone and diacetic acid which have been shown to be poisonous and the cause of diabetic coma. Careful work has been done also on the specific gravity of the blood, in the determination of its exact alkalinity and its osmotic tension.

In recent years the newly discovered properties of blood serum in connection with the production of immunity and its agglutinative action on specific bacteria, infecting the normal body, have given to the blood a prominence in diagnosis and therapy which is shared by no other tissue.

That many more untrodden paths are just ahead in this field of investigation, the work of Ehrlich and others leads us confidently to anticipate.

Much of the recent work just suggested has been possible only in laboratories equipped with expensive apparatus and has required for its performance considerable special knowledge not possessed by the practicing physician. It is rather to the study of the *formed* elements of the blood, to the con-

[1] Paper read at the 104th Annual Meeting of the Medical and Chirurgical Faculty of Maryland, April 24, 1902.

sideration of the number, size and appearance of the red and white cells that he has devoted most attention. Naturally the path has been pointed out step by step by laboratory men, who as skirmishers have blazed the way through the wilderness, in suggesting new stains and better methods to the great army of practitioners following after, and eager for more light in their conflict against disease. In this way a blood examination, at least to the extent of a microscopic survey of a specimen of fresh blood, has become almost as customary in hospital and private practice as the use of the stethoscope or the examination of urine.

The story of the great diagnostic help of even this hasty method need not be here repeated. The medical journals have for several years been eloquent witnesses to the value of a blood examination in many of the maladies common in both medicine and surgery. By means of the fresh preparation referred to, almost invaluable information can be obtained as to the size and color index of the red corpuscles, the relative number of white cells can be roughly estimated with a little practice, and the presence or absence of blood diseases, as anæmia or leukæmia, can be determined. Of more importance still, such an examination should enable one to detect the malarial parasite, if present, and so relieve this interesting plasmodium from the odium of producing every disease which baffles the diagnostic acumen of the doctor.

It is in relation to affections other than that of the blood itself, that the enumeration of the white cells together with a differential count as to the exact percentage of each variety of cell, is of more general diagnostic importance. That the leucocytes are reduced in number in typhoid fever, malaria, miliary tuberculosis and several other affections and increased in pneumonia, bronchitis, appendicitis and other inflammatory processes, is now well known. Although information obtained through this blood count must be weighed in the balance with that from other sources, a knowledge of the number and variety of the white cells and the rapidity of their increase or decrease when rightly interpreted, often affords most valuable information concerning the condition of the patient.

It is rather strange that while the counting of the leucocytes has been employed for years in the practice of medicine among adults, similar methods are not so generally in vogue in pediatrics. This is the more remarkable because in this field of medicine the physician cannot obtain information from the patient concerning the exact subjective symptoms, but must depend almost entirely upon objective signs and the result of his own examination. *A priori* one would think that a knowledge of the blood condition of his patient would be sought early by the pediatrician in the examination of his case, though there are several important differences between the normal condition of the blood in early, as compared with that in later life, which must be appreciated before the examination of the blood of children can be made of much value. It has long been known that the number of red corpuscles is considerably larger in the new born than in the adult; the average of several investigators, including Hayem, Otto, Gundobin and Elder and Hutchison and others quoted by Stengel and White[2] is 5,740,080 per cmm. After a few days, according to Schwinge and Gundobin,[3] this number gradually decreases throughout the first year, after which there is an increase up to the eighth or twelfth year when the number becomes that maintained until adult life. Greater irregularities in the size of the red cells during the first stage of life are described by Hayem, Loos and Gundobin. Many writers[4] have called attention to the increased hæmoglobin content and rather high specific gravity of the blood of infants.

The leucocyte count interests us particularly; it ranges at birth from 14,000 to 27,000 cells to the cubic millimeter. There is a decrease during the third and fourth days, after which time for the first year of life a general mean of 10,000 to 15,000 leucocytes per cubic millimeter is maintained.

Hayem states that the count at fifteen months is about 10,000 cells. Head[5] affirms that after the second year in healthy children the number of leucocytes is about that in adult life and that a leucocytosis in a child over two years of age has the same significance as in an adult.

Another interesting difference in the white cells in childhood is their altered differential count. This varies greatly, as reported by several investigators, and the results are rendered somewhat uncertain by the adoption of several systems of classification. Using Ehrlich's well known scheme, Gundobin[6] and other recent writers give the following as normal in infancy:

| | |
|---|---|
| Lymphocytes | 50-66% |
| Polymorphonuclears | 28-40 |

Ehrlich's figures may be taken as standard for an adult; they are:

| | |
|---|---|
| Lymphocytes | 22-25% |
| Large mononuclear and transitional forms | 2-4 |
| Polymorphonuclears | 70-72 |
| Eosinophile cells | 2-4 |

Thus one sees that in childhood the proportion of lymphocytes is usually much increased and that of the polymorphonuclear cells correspondingly diminished. The number of eosinophiles reported by different writers is so various that further investigation is necessary to establish a mean for early childhood.

As one would anticipate, the blood of infants is in a state of less stable equilibrium than that of adult life. The organism is nearer its embryonic period and the blood-forming centers in the bone marrow and lymph glands are in a

[2] University of Penn., Med. Bull., Vol 14, 1901, p. 310.
[3] Loc. cit. p. 312.
[4] A. Monti, Das Blut und seiner Erkrankungen. Pages 572 and 582.
[5] Arch. of Ped. Vol. 19, 1902, p. 254.
[6] Jahrbuch f. Kinderheilk. vol. xxxv, 1893.

state more responsive to stimulation than in later years. Thus the well known digestive leucocytosis is more marked in infancy than at any other time; an increase of 2000 to 4000 leucocytes has been noted after the ingestion of food. So too there is a quicker response after hæmorrhage, and anæmias of only moderate grade are associated with nucleated red cells and myelocytes in the circulating blood. This and similar factors must be reckoned with in attempting to form an idea of any changed condition in the blood of an infant in the course of a disease. Such difficulties should spur one on to greater efforts to place more counts on record and as the tables grow, it is to be hoped that a number of deductions, helpful in the diagnosis of many of the maladies common in infancy may be possible.

Of all the diseases of infancy none is more deadly in its results nor has so defied the medical profession in their efforts to determine its etiology and proper treatment than the group of closely allied ailments classed together as the "summer diarrhœas." The mortality in our large cities from this cause is hardly appreciated by the physician or layman. Thus in Baltimore in the year 1901 the total mortality of children under five years was 2552, of this number the deaths from intestinal diseases was 732, that is nearly 30 per cent of the total death rate among children was due to diarrhœal diseases. It is particularly fitting therefore to study summer diarrhœa from every possible standpoint and the consideration of the leucocytes, although developing no new or startling facts, will at least have a negative value. It is surprising how few reliable observations there are upon this important subject. Guffer[7] in 1876 found that in chronic atrophy there was a decrease in the number of red cells and an increase in the number of leucocytes. Parrot later made a similar observation. Fischl[8] in a valuable contribution on the study of blood in infants asserts that inflammation of the intestinal tract is accompanied by leucocytosis and that the *lymphoid* cells are particularly increased. A year later Weiss[9] reported a leucocytosis in eight cases with a similar increase in the small round cells which he thought to be due to a stimulation of the lymphoid apparatus of the intestine. These results, although probably erroneous, have been transferred to several text-books on the blood.[10] In the same year Gundobin[11] reported twelve cases of gastrointestinal catarrh in children in which he found a leucocytosis and an increase in the overripe elements, the form in Uskoff's scheme corresponding to the polymorphonuclear cells in Ehrlich's classification of leucocytes.

A later series of twenty cases is reported by d'Olandi[12] in 1899. Most of his patients suffered from chronic forms of enteritis, secondary often to rickets. He observes usually a moderate leucocytosis and a differential count showed an increase in forms which correspond to the polymorphonuclear variety in Ehrlich's classification.

The most complete study of the leucocytes in diseases of the digestive tract in infants appeared in April of last year by Alfred Japha[13] from Heubner's clinic in Berlin. In order to establish a standard for comparison Japha counted the leucocytes many times in a series of twenty-two children under one year of age who were well or suffering from mild illnesses not of the intestinal tract. He found on taking the average of his count the following results:

Leucocytes .....13,560

Differential count:

Lymphocytes .....54%
Large mononuclear cells ..... 4
Polymorphonuclear cells .....42

His results showed considerable variations, but that age, weight and temperature within limits, made no difference. The increased leucocytosis in childhood, he points out, is due to the large percentage of lymphocytic cells.

He then began a series of counts of the leucocytes in the blood of children who were suffering at the time of investigation from dyspepsia or colic; these showed no marked change from his established standards either in the number of leucocytes or in their differentiation into groups. Another series of children suffering from chronic dyspepsia or atrophy presented a similar leucocytic picture. He then divided the cases remaining into three groups:

1. Gastrointestinal catarrh—characterized by foul mucous stools and fever.

2. Follicular enteritis. The cases were many of them fatal. There was rapid wasting with or without fever. The stools contained mucus and blood and often streptococci were demonstrated.

3. Cholera infantum. These cases showed all the symptoms of acute intoxication. Nearly all of them ended fatally.

The leucocyte count in series 1, gastrointestinal catarrh—showed leucocytes varying from 10,300 to 36,000. On differential count an increase in the percentage of the polymorphonuclear leucocytes was demonstrated. They varied in this group from 47% to 55%, while the lymphocytes were reduced to from 38% to 51%.

In group 2, follicular enteritis, this increase in the percentage of polymorphonuclear cells was also noticed. The total number of leucocytes varied within wide limits, depending apparently upon the activity of the body in resisting infection and upon the concentration of the blood. Thus in one case there were but 15,000 white cells while in another there were 38,000. The percentage of polymorphonuclear cells varied from 40% to 75%, average about 60%, and that of the lymphocytes from 18% to 50%, average about 35%.

[7] Revue mensuelle 1876. Cited by Fischl.
[8] Zeitschr. f. Heilkund. 1892.
[9] Jahrbuch f. Kinderheilk. vol. xxxv, 1893.
[10] Ewing, Clinical Pathology of the Blood, p. 344.
[11] Loc. cit.
[12] Rev. Mens d. mal. de l'enf., Jouillet, 1899.
[13] Jahrbuch f. Kinderheilk., vol. liii, 1901. p. 179.

GROUP A.—DYSPEPSIA.

| Name. | Age. | Duration of disease. * | Leucocytes. | Polymorphonucleears. | Small mononucleears. | Large mononucleears and transitionals. | Eosinophiles. | Myelocytes. | Character of stools. | Results. | Remarks. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Annie Ehm, I..... | 6 mos. | 5 days | 13,900 | 37.8% | 39. % | 21.2% | 2. % | .0 % | Fluid, some mucus. | Well. | Onset with numerous loose stools, vomiting. Mild case. |
| Bertha Amend, II.... | 14 mos. | 6 days | 36,500 | 39.2 | 41.8 | 18.6 | .4 | .0 | Semi-fluid, no mucus. | Well. | Onset with vomiting and offensive stools. No blood. |
| Margaret Pierce, III.. | 4 mos. | 16 days | 13,500 | 19.8 | 64. | 14.6 | 1. | .8 | Fluid, no mucus, no curds. | Well. | Onset 2 weeks before with loose bowels, some fever. Child admitted late in disease. |

GROUP B.—DYSPEPTIC DIARRHŒA.

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Katherine Moore, I... | 2 yrs. | 10 days | 24,000 | 66.2 | 17. | 13.4 | 2.8 | .4 | Pasty, yellow, casein and blood. | Well. | Mild case, child about convalescent. |
| Leslie Keller, II..... | 5 mos. | .... | .... | 39.8 | 38.2 | 20.2 | 1.2 | .6 | Yellowish green, mucus. | Improved. | Irregular bowels since birth. No vomiting or fever. |
| Elmer Buenger, III... | 14 mos. | 24 days | 7,000 | 50.2 | 20.2 | 28.6 | 1. | .0 | Watery, greenish mucus. | Improved. | Readmitted with history of blood in stools and irregular bowels for three weeks. |
| Adeline Turk, IV.... | 20 mos. | 11 days | 21,000 | 63.2 | 26.6 | 8.8 | .4 | 1. | Dark, semi-fluid, no lumps. | Improved. | Frequent watery stools, great prostration, blood once. Very severe case. High fever. |
| Estella Wise, V..... | 13 mos. | .... | .... | 41.2 | 37.2 | 16.6 | 3.4 | .0 | Curds, no mucus. | Well. | Sharp attack, no blood in stools, child seen late in disease. |

GROUP C.—ILEO-COLITIS.

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Lydia Seehagen, I.... | 9 mos. | 5 days | 16,300 | 63.8 | 9.6 | 26.2 | .4 | .0 | Yellowish green, mucus. | Improved. | Child in poor condition when admitted. Very ill while in hospital. |
| Marion Sykes, II..... | 7 mos. | 14 days | 11,500 | 63. | 23. | 10.6 | 2.8 | .6 | Curds, mucus, some blood. | Unimproved. | Sudden onset, blood in stools, no vomiting, no fever. |
| Charles Powell, III... | 6 mos. | 5 wks. | 27,600 | 78. | 9.6 | 10.6 | .0 | 1.8 | Fluid, light green. | Died. | History of blood in stools. Onset 2 weeks. Emaciated child. In hospital 3 weeks, unable to retain food. Malnutrition. Autopsy. |
| Barrett Baum, IV.... | 7 mos. | 6 days | 41,000 | 78.4 | 14.6 | 6.4 | .6 | .0 | Mucus, traces of blood. | Died. | Marked prostration. Ulcerative colitis found at autopsy. |
| Bennie Ambrose, V.. | 1½ yrs. | 13 days | 58,000 | 72.4 | 19.6 | 5. | 1.2 | .0<br>1 normoblast | Fluid, mucus and pus. | Unimproved. | Onset with mucus and blood in stools. |
| Charles Graves, VI... | 1 yr. | 14 days | 14,000 | 56.3 | 33.6 | 10. | .0 | .0 | Blood and mucus. | Died. | Autopsy showed ulceration of colon. |
| Charlie Zelinka, VII.. | 4 mos. | 12das.(?) | 27,000 | 75.2 | 14.2 | 10.6 | .0 | .0 | Fluid, no mucus, no curds. | Died. | Vomiting, blood in stools. Autopsy showed ulceration of colon. |
| Alice Constandt, VIII | 1 yr. | 4 wks. | 33,300 | 59.4 | 24.4 | 15.3 | .3 | .0 | Mucus, no blood. | Died. | Autopsy showed ulceration of lower decending colon. |
| Hammond Rice, IX... | 2 yrs. | 6 wks. | 14,100 | 51.4 | 31.2 | 17. | .4 | .0 | Semi-fluid, mucus. | Well. | Onset with mucus and blood in stools, marked emaciation. |
| Isadour Rosenthal, X | 2⅓ yrs. | 6 days | .... | 76.6 | 7. | 15. | 1.4 | .0 | Blood and mucus. | Improved. | |

GROUP D.—CHOLERA INFANTUM.

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Margaret Ritter, I.... | 11 mos. | 2 days | .... | 76.4 | 13.4 | 9.8 | .4 | .0 | Fluid, blood. | Died. | Treated for 1 mo. for dyspeptic diarrhœa. Suddenly developed symptons of intense toxemia. Rickets. |

GROUP E.—INFANTILE ATROPHY.

| Name. | Age. | Duration of disease. | Leucocytes. | Polymorphonuclears. | Small mononuclears | Large mononuclears and transitionals. | Eosinophiles. | Myelocytes. | Character of stools. | Results. | Remarks. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Thomas Johnson, I.. | 4 mos. | 25 days | 30,000 | 40.6 | 45.6 | 12.4 | 1.4 | .0 | Small homogeneous. Occasional trace of mucus. | Died. | Child suddenly removed from breast because of illness of mother. |
| Margaret Herold, II.. | 3 mos. | 40 days | 13,600 | 45.4 | 31.8 | 20.4 | .8 | 1.4 | Dark green, semi-fluid. Occasionally mucus. | Died. | Child lost weight from age of 2 mos. condensed milk feeding. Rickets. |
| Helen Taylor, III.... | 3 mos. | 42 days | 18,600 | 52.2 | 38.2 | 8.4 | .2 | 1. | Semi-fluid, greenish, trace of mucus. | Improved. | |

GROUP F.—INFANTILE ATROPHY COMPLICATED.

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Mary Blackwood, I... | 7 mos. | 40–45 days | 13,000 | 74.8 | 17.8 | .7 | .2 | 1.2 10 normoblasts. | Large, viscid, fairly homogeneous. | Died. | Colitis found at autopsy. Stools just before death contained blood. |
| Lilian Davies, II..... | 5 mos. | .... | .... | 67.8 | 20. | 9.4 | .6 | 2.2 | Fluid, greenish, some mucus. | Died. | Steady loss in weight from onset. Peculiar dark bronzing of skin. No autopsy. |
| Jane Viszkiuskao, III.. | 4 mos. | 60 days | 24,000 | 69.4 | 15. | 14.2 | .4 | 1. | Yellowish green, semi-fluid. Fairly homogeneous. | Died. | Steady loss in weight. Autopsy showed mild colitis. No extensive ulceration. |

* By "Duration of Disease" is meant from time of onset to time when blood was taken.

In the last group, 3, comprising the cholera infantum cases, the leucocytosis was more constant, the white blood corpuscles varying from 51,000 to 54,000 per cubic millimeter. The polymorphonuclear cells averaged about 65% and the lymphocytes about 25%, although there were marked differences in the individual cases.

These results correspond so closely to a series of counts made by one of us last summer at The Thomas Wilson Sanitarium that we venture to incorporate them in the nature of a preliminary report, as it is hoped that a more complete investigation can be conducted during the coming season. Our cases, twenty-four in number, are briefly summarized in the accompanying table.

The blood was collected in the usual manner on cover-slips and fixed by heating over a copper bar or in absolute alcohol and ether, and then stained by Ehrlich's triple stain. A number of the specimens were air dried and stained with Jenner's stain, which gave excellent results. At the time of obtaining the blood for the specimens the leucocyte count was made. All our patients suffered from some form of digestive disturbance; most of them were extremely ill and were seen rather late in the course of disease.

They can be arranged according to their symptoms into groups corresponding with those of Japha, although the several grades of the affection merge, the one into the other, and the division line must be to some extent artificial.

The blood of several well babies was counted for comparison; it averaged about as follows:

| | |
|---|---|
| Polymorphonuclears | 35% |
| Small mononuclears | 50 |
| Large mononuclears | 11 |
| Transitionals | 3 |
| Eosinophiles | 1 |

Three cases were counted which belonged to group A, in which the disturbances were of mild grade; they resulted thus: The leucocytes varied from 13,500 to 36,000.

Differential count was as follows:

| | |
|---|---|
| Polymorphonuclears | 37.8% |
| Small mononuclears | 39 |
| Large mononuclears | 19.2 |
| Transitionals | 2 |
| Eosinophiles | 2 |

In this group the normal differential count was but slightly altered.

Group B. Dyspeptic fomental diarrhœa; here the leucocytosis was of mild grade, about 21,000. The analysis of the count shows an increase of the polymorphonuclear forms as follows:

| | |
|---|---|
| Polymorphonuclear leucocytes | 39 to 63% |
| Large mononuclear leucocytes | 8 to 26 |
| Transitionals | .4 to 2 |
| Eosinophiles | .4 to 3.4 |

The next group, the largest, group C, comprises those cases where symptoms or autopsy revealed marked inflammatory changes in the intestinal wall. The leucocytes varied from 16,000 to 58,000.

| | |
|---|---|
| Polymorphonuclear leucocytes | 56-78% |
| Small mononuclear leucocytes | 7-33 |
| Large mononuclear leucocytes | 3-21 |
| Transitionals | 0- .4 |
| Eosinophiles | 0- 1.4 |

Group D. A case which showed symptoms of acute intoxication and should be classed as cholera infantum and had practically an identical blood count.

In group E are gathered those cases of infantile atrophy without many symptoms of digestive disturbances. Here the leucocyte count varied from 13,600 to 20,000, distributed as follows:

| | |
|---|---|
| Polymorphonuclear leucocytes | 40-52% |
| Small mononuclear leucocytes | 31-45.6 |
| Large mononuclear leucocytes | 8-18 |
| Transitionals | 0- 2.7 |
| Eosinophiles | .2- 1.4 |

Group F included those cases of atrophy or marasmus in which usually as a terminal infection there is in addition, inflammation of the intestine. In these cases there was little increase in the leucocyte count which varied from 13,000 to 24,000. The differential count was as follows:

| | |
|---|---|
| Polymorphonuclear leucocytes | 57-74% |
| Small mononuclear leucocytes | 15-20 |
| Large mononuclear leucocytes | 6-13 |
| Transitionals | 4- .8 |
| Eosinophiles | 2- .6 |

In every case but two, 500 leucocytes were counted.

It will be noticed that the count obtained in a number of the cases, e. g., group A all cases, group B cases 2 and 3, group C case 1, group E case 2, showed a large percentage of large mononuclear cells. This apparent increase may be explained by the following facts. In infants' blood the different forms of leucocytes are not so sharply defined as in the blood of adults, and so there are constantly seen cells of a mononuclear variety which are neither lymphocytes nor typical large mononuclear leucocytes, and the group in which the somewhat doubtful cell is placed must be determined by the personal equation of the counter. All mononuclear cells larger than the average sized polymorphonuclear leucocyte were called by us large mononuclear cells. It is to be noted, as seen in the table, that the cases of the highest percentage of the large mononuclear cells as a rule did well, whereas in those cases in which the percentage of these cells was low either died or were unimproved. However a much larger series of cases must be taken before anything conclusive as to the prognosis can be drawn from these findings. Myelocytes were found in only a few of the cases and the percentage was never high. No importance can be attached to their presence in our series. In only two cases were nucleated red blood cells seen and these were normoblasts (group C, case V; group F, case I). In a number of cases no eosinophile cells were seen in counting 500 leucocytes. This tallies with the observations made by several observers tending to show that these cells, as far as known, have little significance in these disorders.

A comparison of our findings with those of Japha indicate that leucocytosis in cases of this nature is no index of the severity of the attack.

As pointed out by Rieder,[14] the following varieties of leucocytosis produced by pathological influences may be distinguished.

1. Inflammatory.
2. Toxic.
3. Post hæmorrhagic.
4. Cachectic.
5. Agonal or premortal.

In summer diarrhœa the leucocytes are similarly increased in the ulcerated inflammation of the intestine and in acute autointoxication, and their simple enumeration affords little aid to diagnosis. Their number is also affected by other factors, such as the specific gravity of the blood, the resistance of the patient, etc., which factors are not as yet thoroughly understood.

Of more moment than the number of the white cells is their differential count. The results enumerated above would seem to indicate that the more severe the infection the greater the number of polymorphonuclear leucocytes in relation to the mononuclear forms.

Our conclusions may be briefly summarized as follows:

1. A differential count of leucocytes in the blood of well children under two years of age, when compared with the blood of adults, shows that there is a relative increase in the small mononuclear elements and a decrease in the number of polymorphonuclear cells.

2. In the summer diarrhœas of infants the number of leucocytes in the blood is usually increased but the count of the white cells varies within such wide limits, even in the milder forms of the affection, that a high or low leucocytosis cannot be regarded as of diagnostic value.

3. In the simple dyspepsias of childhood a differential count of the leucocytes does not show any marked variation from that of a healthy infant, but as the cases become more severe in type there is apparently a progressive increase in the polymorphonuclear neutrophile cells and a decrease in those of the small mononuclear variety, thus presenting a picture more like that of adult blood.

4. As pointed out by Japha, the polymorphonuclear leucocytosis is an indication of an intoxication with decomposition products in the intestine or of the toxins of pathological bacteria; i. e., it takes place both in the cases of acute intestinal poisoning and in the more severe forms of ileocolitis.

5. The cases of simple infantile atrophy present a nearly normal differential leucocyte count, but it would seem that an increase of the polymorphonuclear cells may indicate the setting in of an inflammatory intestinal complication.

[14] Quoted by Monti, Loc. cit., p. 594.

# TYPHOID FEVER: REPORT OF A CASE WITH THREE RELAPSES. REMARKS.

BY LOUIS M. WARFIELD, M. D.,

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CASE.—*Typhoid fever of long duration. Severe initial attack, hemorrhages; three relapses and three recrudescences; recovery.*

L. D., white, female æt. 12, Hosp. No. 35,764, was admitted August 5, 1901, to the Johns Hopkins Hospital in the service of Dr. Osler, on the 4th day of disease, complaining of pain in the stomach, headache and fever. Beyond a history of consumption in the family, the family history is unimportant. She herself had previously been fairly strong and healthy. She had had none of the acute infectious diseases except measles and whooping cough. There was a history of chills and fever, 14 months ago, lasting about one week. Menstruation has not yet been established. For two months past she has had no appetite, has felt tired out and has complained continually of headache and backache. Since June she has had a dry hacking cough without expectoration and her cheeks have been constantly flushed. She had no night sweats, chills, or epistaxis. Since August 2 she has been in bed with high fever. For several days before her admission she complained of pain in the abdomen and the night before admission she was delirious. She had lost considerable flesh and strength during the past two months. She drank unboiled hydrant water. No one else in the house was ill.

*Condition on Admission.*—Fairly well nourished child. Examination of lungs and heart showed nothing abnormal. Pulse 92 to the minute, not dicrotic, regular. Abdomen not distended, respiratory movements free throughout. No rose spots. Spleen just palpable when she lies on her right side. No abdominal tenderness. Hepatic flatness just reaches the costal margin in the right mammary line. No delirium.

There was some diarrhœa on admission, the stools being "pea-soup" in consistency, but her bowels soon became fairly regular and remained so throughout the whole illness. The urine showed a marked diazo-reaction. There were no albumin and casts. The examination of a fresh blood smear showed no malarial parasites but a curious vacuolic degeneration of the leucocytes was noted. The count per cmm. was: erythrocytes 4,956,000, leucocytes 12,600, hemoglobin 82 per cent. From blood cultures taken on August 6 a pure culture of *B. typhosus* was obtained. On August 7 rose spots were found over the abdomen. On August 8 the Gruber-Widal reaction was positive in dilution of 1:50.

The patient was given ice sponges for three days, then put in a tub bath at 85° every three hours whenever her temperature reached 102.5° or over. She did very well up to August 15, at 9 a. m., when she had a hemorrhage of bright blood, about 150 cc., followed by a continuous bleeding, amounting in all to 500 cc. She became slightly collapsed. Her pulse became imperceptible after the last hemorrhage. There was some pain in the abdomen. That night she had two more hemorrhages, losing in all about 760 cc. of blood. She was infused with normal salt solution and given a 2 per cent solution of gelatin subcutaneously. In addition she had morphia and lead and opium. She was infused again at night as her condition was very grave. An ice bag was kept over her abdomen and all nourishment was ordered to be withheld for 24 hours. The leucocytes, which had been 4000-7000, now rose to 12,000, her red blood corpuscles were 4,484,000, and hemoglobin 78 per cent. She rallied well and her pulse had improved markedly when on August 16, she became very restless and somewhat irrational. The abdomen was tender but not until afternoon of August 16 did she complain of severe abdominal pain. At that time there was exquisite tenderness in the lower quadrant of the abdomen with definite rigidity and muscle spasm, but on closer examination similar tenderness was found over her thigh and it was not long before the muscle spasm and rigidity had completely disappeared. Her condition remained about the same throughout afternoon and night. She had voided urine in the meantime and when seen at 11 p. m. by Dr. Futcher the note was as follows: "Her features are distinctly drawn at times. The abdomen is not distended. Respiratory movements if anything are slightly less marked than at 6 o'clock. She cries out at times with pain which it is difficult to get her to locate owing to her semidelirious condition. The slightest pressure over the right lumbar and iliac regions causes acute pain and there are definite muscle rigidity and spasm on the right side but none on the left. Liver dulness still reaches the costal margin. It is not possible to test for movable dulness in the flanks. She has not vomited. The pulse volume is not quite so good as it was earlier in the day. It has continued practically 120 since 6 o'clock." Owing to the variability of the pain, the similar pain over the thigh together with the fact that her condition grew no worse, the symptoms were considered to be due to a neurotic condition. A blood count made during the day showed red blood corpuscles 3,292,000, white blood corpuscles 4000, hemoglobin 40 per cent.

August 17. Her condition decidedly better but she is still delirious. Her temperature continued high (see chart). The pulse improved and abdominal tenderness was not nearly so marked. Her leucocytes were 3900 and hemoglobin 40 per cent. She developed a cough during the next few days and a bed sore over sacrum.

On September 2, the thirty-second day of her illness, her

temperature touched normal. From that date until September 27 it was practically normal, showing an occasional rise to 99°. She seemed apparently quite well, and was about to be discharged when suddenly on September 28 her temperature rose to 103.2° and she had headache but no diarrhœa. She looked rather ill; her tongue was slightly coated, her pulse 100 and not dicrotic. The spleen was not palpable and no rose spots were seen on the abdomen. On October 3 rose spots were seen and the spleen was palpable. Blood cultures were taken again and *B. typhosus* was obtained in pure culture. The urine showed considerable albumin and quantities of pus cells and the diazo-reaction which had not been obtained since the primary attack of fever, was again positive. A blood count showed red blood corpuscles 3,988,000, white blood corpuscles 4600 and hemoglobin 58 per cent. Her condition was good; she suffered no pain and on October 3, the sixty-third day of her stay in hospital and sixth day of her relapse, her temperature touched normal. It oscillated slightly above and below normal for four days, during all of which time the spleen was palpable but becoming smaller every day. On October 8 her temperature sudenly rose to 103.7°. On October 12 there was a sharp intercurrent rise and the patient appeared quite ill. Her leucocytes now rose to 12,700 and besides the albumin in the urine, some red cells were seen under the microscope. She complained of slight abdominal pain; spleen readily palpable. Her temperature continued between 101.6° and 104.5° until October 17, when it touched normal again. From October 18 to 20 she was afebrile. Her pulse was slow and of good volume and tension. October 19 her spleen was just palpable. From October 20 to 26 she had another febrile period during which rose spots appeared on the abdomen but the spleen was not palpable. Her temperature was practically normal until October 31, when it rose to 102.5°. Her leucocytes, which had, since the last rise, fallen to 7000, rose to 14,500. There were no rose spots but her spleen again became palpable. November 2, rose spots were seen on abdomen. Her temperature showed marked oscillations to November 4. She then appeared in good condition, was quite bright. There was considerable cyanosis of trunk and limbs although her temperature was normal. On November 7 a few fresh rose spots were seen, the spleen, however, was not palpable. There was an irregular temperature, at times reaching 102.6°, but on November 13, with this temperature and a rapid pulse, there were no fresh spots and her spleen was not felt. On November 18 her temperature became normal and remained so for 11 days. She was again apparently well and almost ready to go home. On November 30, the 121st day of her illness and 64 days since the first relapse, she complained of a headache. Her temperature was 100° at 6 a. m., rising at 2 p. m. to 103.7°. She was listless and apparently felt badly. Her pulse was 140, rather small; spleen readily palpable; no rose spots; abdomen natural, not tender. Her temperature remained elevated for 60 hours when it became normal and she passed on to complete recovery. She was discharged December 15 after a residence in the hospital of 136 days.

Relapses in typhoid fever are unfortunately common enough and vary greatly in different places and in different years. Multiple relapses, by which we mean three or more relapses, are however not common. Da Costa[1] mentions in a clinical lecture that he has seen two cases with five relapses each, both of whom recovered. Jaccoud and Netter[2] each report a case with five relapses. No cases with more than five relapses could be found in the literature.

Carslaw[3] reports a case with four distinct relapses, lasting from August 10 to March 6, when the patient was discharged well. The initial attack lasted 34 days. The patient was very ill, had hemorrhages from the bowels and was *in extremis*. She survived and her temperature fell by lysis and was normal for two days. It then rose and she had a relapse lasting 23 days. There was an interval of apyrexia of 15 days when the temperature again rose and patient entered on the second relapse. Rose spots were noted for the first time. This relapse lasted 22 days and was followed by normal temperature for 10 days. There was a third elevation lasting 16 days complicated with *plegmasia alba dolens* of one leg. Again the temperature became normal and remained so for 16 days when she had a fourth relapse lasting 10 days. Recovery was complete.

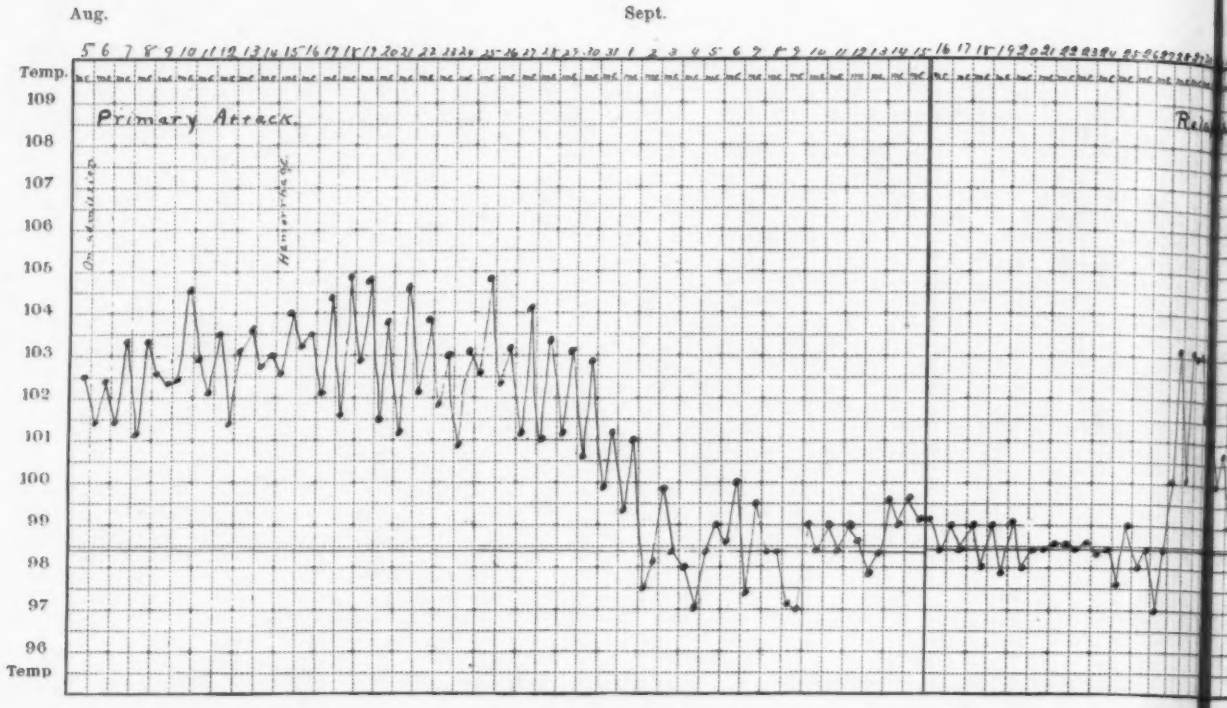
Béna,[4] in his series of 598 cases in Strassburg from 1872-91 and 168 cases in Königsberg from 1877-87, found 79 single relapses, 13 double relapses, 6 with three relapses and one (partially reported only) with five relapses.

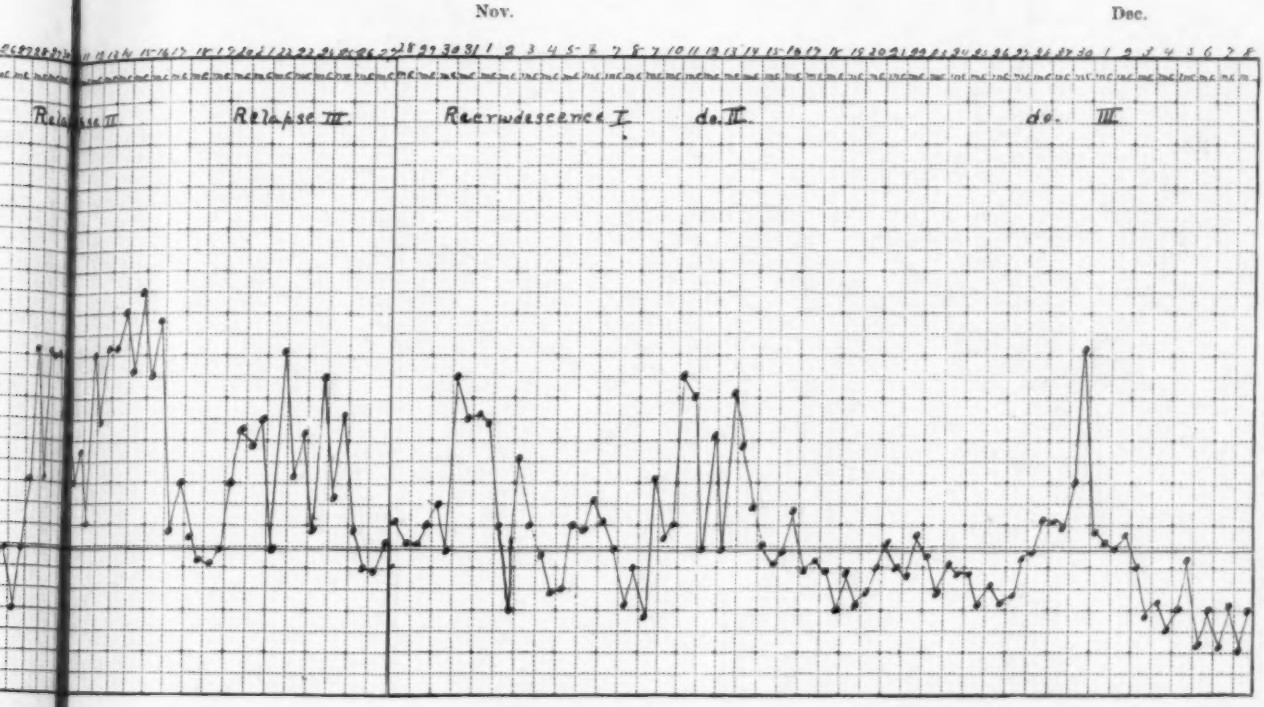
In the Johns Hopkins Hospital Reports, Vol. VIII, p. 437, a protracted case with three relapses is reported. The patient, a woman of 26, had a primary attack in June; her first relapse occurred early in September; her second relapse early in November, the onset being with arthritis, and her case was at first thought to be one of acute articular rheumatism; her third relapse consisting of a fever of 9 days without rose spots or a palpable spleen. Recovery was complete.

That the relapse is much milder and less fatal than the primary attack has long been noted. A most striking series of figures is given by Melville.[5] He saw 295 cases of typhoid fever, 23 or 7.79 per cent had relapse and all the relapsed cases recovered. Of the 295 cases 7 died, a mortality of 2.38 per cent.

There is now considerable unanimity of opinion as to what the terms "relapse," "recrudescence" and "intercurrent relapse" mean. A relapse is never caused by external and exciting causes alone, such as sudden emotion, overfeeding, visits of friends, etc., but it is due to a reinfection of the organism with the typhoid bacillus. Shattuck,[6]

[1] Med. News, Phila., 1893, lxii, 154–156.
[2] Quoted by Hunt. Pract., Lond., 1898, lx, 263.
[3] Lancet, Lond., 1890, ii, 120–122.
[4] Ueber Typhus-recidive. 8° Strassburg, 1893. Inaug. Dis.
[5] Brit. Med. Jour., 1901, i, 952-954.
[6] Bost. Med. & Surg. J., 1889, cxxi, 221–224.


Aug.
Sept.
Temp.
109
108
107
106
105
104
103
102
101
100
99
98
97
96
Temp
Primary Attack.


Nov.
Dec.
Relapse III.
Relapse III.
Recrudescence I.
do. II.
do. III.

discussing relapses, says: "Constipation, nourishment unsuitable in kind or too large in amount, the excitement of a visit, or a number of other causes may produce a return or an exacerbation (*what we call a recrudescence*) of fever: to produce a relapse there must be a re- or auto-infection."

There are certain well-known features of the relapse which may be mentioned. Chief of these are: (1) the shorter course; (2) the milder character as a rule; (3) a low mortality; (4) a more sudden rise of temperature, often reaching its maximum within 48 hours; (5) more often than not a rapid lysis. The fever of the relapse may be higher than that of the initial attack and the patient may be more severely ill. Whether the relapse which follows a severe attack is more severe or milder than one following a mild primary attack or vice versa it seems impossible to say. Nor can we predict from the nature of the primary attack whether or not there will be a relapse. Repeated efforts have been made to collect statistics to show that age, sex, race, time of year, etc., have some relation to relapses but the variations in statistics only show that no definite conclusions can be drawn.[7]

In the case reported the primary attack was severe. It was thought at one time that the bowel had perforated. Upon analyzing the various elevations in temperature it seems probable that the last three elevations were recrudescences rather than relapses. Although in the last one the spleen became palpable, still the transient elevation of temperature, its rapid fall and the rapid convalescence spoke against a true relapse. Also in one of the two short elevations preceding, there was a palpable spleen and a leucocytosis possibly due to cystitis. However, there was no coating of the tongue and the patient did not seem ill. In the recrudescence commencing November 11 it is probable that a soft boiled egg given on the afternoon of the 10th was the cause of a transient rise of temperature without fresh rose spots or enlargement of the spleen. Thus dividing the illness into days we have:

| | |
|---|---|
| Primary attack August 2 to September 2 | 31 days. |
| Apyrexia | 26 " |
| First relapse September 28 to October 3 | 5 " |
| Period of practically normal temperature | 4 " |
| Second relapse October 7 to October 17 | 10 " |
| Apyrexia | 3 " |
| Third relapse October 20 to October 26 | 6 " |
| Apyrexia | 5 " |
| First recrudescence October 31 to November 2 | 2 " |
| Apyrexia | 9 " |
| Second recrudescence November 11 | 1 " |
| Apyrexia | 19 " |
| Third recrudescence November 30 to December 1 | 1 " |

Discharged December 15.

There was a long interval between the initial attack and the first relapse. A short but definite interval between the first and second, and second and third relapses and in the third relapse the temperature rose to within .4° F. of the highest temperature in the primary attack.

The question naturally arises why should a typhoid fever patient have relapses. Pneumonia, scarlet fever and diphtheria do not act thus. This question has attracted attention since Schultz in 1831 described three true relapses in 55 cases of typhoid fever which he thought to be due to overfeeding or exposure to cold. The relapse has been ascribed to one of two conditions, either (1) a second new infection, or (2) the result of the products of infection from the first attack remaining in the organism.

In 1894 Stewart[8] (H. M.) collected and analyzed 40 cases of typhoid fever dead in relapse on whom autopsy was performed. He found that in 34, 85 per cent, of the cases the large intestine contained recent ulcers, while the small intestine showed the presence of recently healed ulcers. In the other 15 per cent there were ulcers both in small and large intestine. On the contrary, of 65 cases dead in primary attack 48, or 75 per cent, showed a healthy large intestine and ulceration in the small intestine. He thought that in the primary illness the small intestine bore the brunt of the attack while in the relapse the large intestine chiefly suffered. Hence he concluded that the relapse was due to a reinfection of the intestine by sloughs derived from some portion above.

The autopsy records of the Johns Hopkins Hospital were analyzed with regard to this point. 68 autopsies were found to March 15, 1902, of which 2 cases died during a relapse. Of 66 cases then there was ulceration in the ileum alone in 21 (31.8 per cent); in the colon alone in 1 case; ulcers in both small and large intestine were found in 41 (62.1 per cent), of which 3 cases had very slight ulceration in the ileum and extensive ulceration in the colon; 1 case with ulcers in the ileum and enlarged follicles in the colon; 3 cases without visible ulceration. Perforation occurred 10 times, the ileum being perforated nine times, the sigmoid flexure once. Of the 2 cases of relapse both had ulcers in the ileum, in one case healing in places. Neither case had an ulcer below the ileocecal valve. In other words, in two-thirds of the cases which died in the primary attack an ulceration of the colon was found. These figures show quite conclusively that such a theory as the one advanced above is inadequate to explain why relapses occur.

Within the past year a new theory of the etiology of the relapse in typhoid fever has been advanced by Durham.[9] When an animal dies with its blood containing a quantity of specific antitoxin substances he considers that its death may have been due to the action of some toxin or variety of toxin against which no antitoxin has been manufactured in the serum. He assumes that no infection is a simple process in which all organisms of the same species are iden-

[7] For large series of statistics see Béna, loc. cit. and R. Lohse, Ueber das Recidive des Ileotyphus. Freiburg i. Br. 1898.

[8] Relapses in Typhoid Fever. Pract. Lond., 1894, lii, 184.

[9] Jour. Path. and Bact. vii, 1901, p. 240.

tical, but an infection is a complex phenomenon, due to the infection with the varieties and subvarieties of the infecting agent, no one of which being identical with nor equivalent to any other one. Should the groups be more or less equivalent we should have a normal, isozymic infection; should one or more varieties preponderate we should have an abnormal or anisozymic infection. Each variety and subvariety is then assumed to have its corresponding antibody formed in the blood.

This is quite consistent with and follows from the results of the recent work on hemolysis and bacteriolysis where apparently there are innumerable antibodies, everyone called forth by its specific toxin.

Durham says further that probably a pure infection never occurs, hence every infection consists of an infection with a number of varieties and the sum of the forces acting on the organism calls forth a quantity of responses and consequently a complex body is the result. If the different antibodies are called forth in sufficient number to take care of the toxins of the different varieties the organism recovers from the infection and no relapse occurs. If, on the other hand, the varieties are remote, there will be a preponderance of certain groups of antibodies which react only with the corresponding varieties of the infecting agent. There will also be a slight production of antibodies corresponding to the groups of the bacterium which have been, so to speak, overgrown. If, now, these latter bacteria start to grow, the organism will be reinfected as there are no antitoxins in the blood corresponding to these toxins. As these groups were fewer in number and were not so virulent as the groups causing the primary attack, so the relapse will be both shorter and of a milder character than the initial attack.

That this is not theory alone is borne out by numerous experimental observations and by analogy. It has been proved that there are differences in bacilli derived from the same source by testing them with different sera.[10] Durham has shown[11] also that "not only are there quantitative variations in the amount of protective antibodies in the sera taken from typhoid fever convalescents, but also that there are apparently qualitative differences as well." These differences in the bacilli derived from the same source are too subtle to be shown in cultural media. It is only by their serum reactions that these differences can be made out and studied.

Again, we have a familiar example of variety in the behavior of the streptococcus. At one time erysipelas, at another time deep cellulitis, again rapid general infection and death may develop while culturally no differences can be shown in the cocci present. It has been repeatedly proved that every one of the numerous known varieties of streptococci has its own protective serum. Hence the divergent results obtained by those who have used antistreptococcic serum on patients infected with the coccus. The serum that would cure one patient would have no effect on another suffering from an infection due to a different variety.

It would seem therefore that Durham has sufficient grounds on which to base his hypothesis. The theory is more adequate than any yet advanced and as a working basis it suffices. On this theory multiple relapses can also quite readily be explained. For if every infection is complex, several groups of the infecting agent may cause the primary attack, several other groups the first relapse, several other non-identical groups the second relapse and so on. And the patient is liable to a reinfection as long as there are groups of the bacterium to counteract the toxic action of which no antitoxins have been formed in the blood or other tissues. It remains now for cumulative evidence to establish whether or not it is a pure hypothesis.

March 28, 1902.

[10] Pfeiffer and Kohl, Zeitschr. f. Hyg. u. Infectious krank., Leipzig, 1886, Bd. xxi, S. 203. Quoted by Durham.

[11] Jour. Path. and Bact., 1897, iv.

# THE CLINICAL VALUE OF OLIVER'S HAEMOCYTOMETER.[1]

By Walter Baumgarten, A. B., M. D.

*(From the Clinical Laboratory of the Johns Hopkins University.)*

The object of this report is to call attention to certain sources of error in Oliver's haemocytometer, which indicate that it may be well to accept with some reserve the opinion that the instrument is satisfactory and accurate for estimating the number of red blood corpuscles in disease.

The construction of this instrument is based upon the fact that when a flame is viewed through a glass tube, it appears as a bright transverse line consisting of numerous small images of itself. When the tube so used is filled with a fluid containing small particles in suspension, as for instance, red blood corpuscles, the interference with the transmission of light produced by them obliterates the line of images until a certain dilution of the mixture is reached. Oliver found that, using a tube of definite dimensions, a constant quantity of normal blood, and a definite diluting fluid, the point at which the line of images appeared could be determined within less than 1 per cent, and that the same was true for all variations in the number of corpuscles within normal limits. Taking 5,000,000 corpuscles as 100 per cent,

[1] Oliver, G., British Med. J., i, p. 1493, 1896.

the tube was then graduated uniformly from this point to the bottom, which was taken as zero.

Oliver himself suggests the instrument as useful only in determining the number of red blood corpuscles in normal blood, and as applicable to physiological investigations rather than to clinical work in general. From the standpoint of the clinician he classes it with the haematocrit as a volumetric method, with which it shares the errors due to variations in the size of the corpuscle. In spite of the limitations so set upon it by Oliver, the instrument has been introduced into clinical work by others[2] with results which are alleged to agree very closely with actual enumerations by the Thoma-Zeiss instrument.

On putting the instrument to practical use in the clinical laboratory, Oliver's opinion as to its inadequacy in the anaemias was borne out, namely, that, compared to the Thoma-Zeiss count, its results varied as much as 20 to 30 per cent and more (both too high and too low). At Dr. Emerson's suggestion, and with his aid, the influence of certain elements of error entering into the determination was investigated.

In addition to the error due to variation in the size of the red corpuscles, an error is undoubtedly introduced by the coagulation of the proteids of the blood plasma by the mercuric chloride of Hayem's solution, which is used as the diluting fluid. Oliver minimizes this, and states that as much as 50 cmm. of serum, or five times as much as the blood-gathering pipette of the instrument contains, produces "the merest haze" when diluted to the 20 per cent mark. A repetition of this experiment gives in our hands a very different result, namely, a dense white coagulum is immediately formed, which interferes with the appearance of the reading until the dilution is carried to the 52 per cent mark.

Following this out, a single pipetteful of serum was substituted for the larger quantity. A series of observations so carried out demonstrated that a dilution with Hayem's fluid up to the 11 per cent mark was necessary to obtain a reading. This shows clearly that the coagulation of the serum causes an opacity which will be denser the smaller the dilution is, and will tend to disappear as the dilution is increased. The question arises, will this opacity increase the reading of the instrument above the point to which the corpuscles themselves would bring it.

In determining this question, mixtures of a normal blood (containing about 5,000,000 corpuscles per cmm.) and a freshly separated serum from human blood were made by drawing into the blood-gathering pipette varying proportions of blood and serum. Of three such mixtures, the first contained 20 per cent blood and 80 per cent serum, in which the reading should theoretically be obtained at the 20 per cent mark, representing 1,000,000 cells per cmm.; the second contained 40 per cent blood and 60 per cent serum, and should be readable at the 40 per cent mark; the third contained 60 per cent blood and 40 per cent serum, and should read at the 60 per cent mark. The readings, however, were in the first mixture 7 per cent too high, corresponding to an error of 350,000 cells; in the second mixture 5 per cent, or 250,000 cells too high; while in the third mixture the error had practically vanished. This demonstrates that the coagulation of the proteids of the blood increases to some degree the extent to which the dilution must be carried to obtain the appearance of the transverse line of light, and that it forms a positive error.

In addition to the effect of the coagulation of the plasma, there is still another source of error, as Oliver has pointed out, namely, the variation in the size of the corpuscles. For example, even though the number of corpuscles be constant, the larger the corpuscles the greater will be the interference with the light, and the higher the readings obtained. Since the form of the corpuscles is such that changes in volume are due almost entirely to changes in area, and since the area varies with the square of the diameter of the corpuscle, the latter may be taken as an index of the changes in volume, and may be made the basis for calculation.

These two corrections, applied to actual cases, bring the error in the Oliver count, in most cases, within the limits of error of the Thoma-Zeiss instrument, taking this error at 200,000 cells. That the total correction is not more complete is probably to be ascribed to the fact that the graduating of the pipette used for the determination of the error arising from coagulation of the plasma, was crude; and it follows that the figures obtained by it are not perfectly accurate.

To illustrate the results obtained by Oliver's instrument, the following cases may be cited. The figures presented in the first two cases may be regarded as of more than ordinary value, as they are the results obtained from independent observations taken at the same time by a number of individuals; furthermore, they vary from the actual count within the limits of error of the Thoma-Zeiss counter.

TABLE I.

| Oliver. | Thoma-Zeiss. | Difference. |
|---|---|---|
| *Normal Case.* | Count. | |
| 5,550,000 | | 218,000 |
| 5,500,000 | | 168,000 |
| 5,550,000 | | 218,000 |
| 5,500,000 | 5,332,000 | 168,000 |
| 5,475,000 | | 143,000 |
| 5,150,000 | | —182,000 |
| 5,200,000 | | —132,000 |
| *Pernicious Anaemia.* | | |
| Count I. | | |
| 3,900,000 | | 2,175,000 |
| 3,675,000 | 1,725,000 | 1,950,000 |
| 2,850,000 | | 1,125,000 |
| 2,850,000 | | 1,125,000 |
| Count II. | | |
| 2,800,000 | | 1,544,000 |
| 2,900,000 | 1,256,000 | 1,644,000 |
| 2,750,000 | | 1,494,000 |
| 2,775,000 | | 1,519,000 |

[2] Cabot, Clinical Examination of the Blood, Fourth edition, 1901, p. 30.

| Oliver. | Thoma-Zeiss. Count. | Difference. |
|---|---|---|
| *Secondary Anaemia.* | | |
| Case I. 3,050,000 | 3,600,000 | —550,000 |
| " II. 3,050,000 | 3,918,000 | —868,000 |
| " III. 1,650,000 | 2,120,000 | —470,000 |

In a normal case with a Thoma-Zeiss count of 5,332,000 cells, observations were made with Oliver's haemocytometer by seven individuals, which varied from 5,150,000 to 5,550,000, differing from the count by from 132,000 to 218,000 cells. A case of pernicious anaemia with a count of 1,725,000 cells, gave results in the hands of four individuals varying from 2,850,000 to 3,900,000, a positive difference of from 1,125,000 to 2,175,000. The same case a number of days later gave a second count of 1,256,000 cells, while Oliver's instrument read from 2,750,000 to 2,900,000, an excess of 1,494,000 to 1,644,000. In the secondary anaemias Oliver's instrument gives results much below the count, as the three cases in the table demonstrate, namely, a deficit ranging from 470,000 to 868,000 cells.

The correction for the two errors has been made by subtracting from the result given by Oliver's instrument the error due to coagulation of the plasma at the reading in a given case, and then dividing the result by the factor representing the ratio of the square of the measured diameter of the corpuscles to the square of the diameter of the normal corpuscle, that is, of 7.5$\mu$. Working out the first corrected case (pernicious anaemia) in this way (see Table II), the error due to plasma is 330,000, which, subtracted from the Oliver reading (1,150,000) leaves 820,000. The average measured diameter of the red corpuscles was 8.7$\mu$.

TABLE II.

Corrected Readings.

| Oliver. | Thoma-Zeiss. Count. | Difference. | Diameter of Corpuscles. | *Corrected Difference.* |
|---|---|---|---|---|
| *Pernicious Anaemia.* | | | | |
| 1,150,000 | 798,000 | +352,000 | 8.7 $\mu$ | —186,100 |
| *Secondary Anaemia.* | | | | |
| 3,050,000 | 3,918,000 | —868,000 | 6.8 $\mu$ | —198,500 |
| 1,650,000 | 2,120,000 | —470,000 | 6.8 $\mu$ | —412,000 |

so that the ratio becomes $\frac{8.7^2}{7.5^2}$, giving the factor 1.34. Completing the correction, 820,000 divided by this factor gives 611,900 red blood corpuscles,

$$\left[\frac{8.7^2}{7.5^2} = \frac{820{,}000}{x} \quad x = \text{corrected reading},\right]$$

$$1.34x = 820{,}000 \quad = 611{,}900,$$

still leaving a difference of 186,100.

From the figures thus offered it may be seen that in the anaemias Oliver's haemocytometer gives very inaccurate results. The result is open to question in cases giving actual counts even as high as four million (3,918,000), so that this may be regarded as the lower limit of accuracy. Since readings above this point do not convey information of great consequence to the clinician, it may be concluded that Oliver's haemocytometer has very slight value in clinical work.

## THE BOYLSTON PRIZE.

Robert L. Randolph, M. D., Assistant Ophthalmic and Aural Surgeon to the Johns Hopkins Hospital, and Associate Professor of Ophthalmology and Otology in the Johns Hopkins Medical School, has recently received the Boylston Prize for a paper entitled: The Rôle of the Toxins in Inflammations of the Eye. An Experimental Study.

## NOTES ON NEW BOOKS.

**Atlas and Epitome of Otology. By GUSTAV BRÜHL, M. D., of Berlin, with the collaboration of PROF. ADAM POLITZER of Vienna. Edited, with additions, by S. MACCUEN SMITH, M. D., Clinical Professor of Otology, Jefferson Medical College, Philadelphia. With 244 colored figures on 39 lithographic plates, 99 text illustrations, and 292 pages of text. Cloth $3.00 net. (*Philadelphia and London: W. B. Saunders & Co., 1902.*)**

The latest and by no means the least valuable of the excellent series published by Saunders, this volume will receive a particularly cordial greeting because of the scarcity of otologic atlases. Those responsible for its appearance, however, have not depended upon this point to secure its appreciation, but have issued a work which commands the highest praise of those interested in the study or the teaching of otology. A well chosen illustration is valuable in the teaching of any subject and especially when dealing with anatomy does a clear and succinct demonstration enable the student to quickly comprehend the subject. A collection of illustrations such as lies before us is of great value also to the careful surgeon who finds it necessary to frequently refresh his memory of topographical anatomy. The temporal bone is by all odds the most difficult one in the human body to gain a complete and masterful knowledge of, and its variations in form and construction are so nearly innumerable as to require continuous study and constant watchfulness on the part of the operator.

Dr. Brühl appears to have had the privilege of choosing specimens *ad libitum* from Prof. Politzer's magnificent collection and he is certainly to be congratulated upon the excellent judgment displayed in his selections. The lithographic work has been most admirably performed and one can scarcely conceive any improvement upon it. The text descriptive of the figures is well arranged to bring out every point of importance in the illustration and render the whole perfectly clear. It is hardly necessary to speak of any plates in particular, they are all good, but those illustrating pathological conditions of the middle ear and its adjoining structures are perhaps the most important and the best prepared.

The second half of the book is a condensed treatise on diseases of the ear, intended especially for the student, and the author has succeeded marvelously well in compressing a comprehensive knowledge of his subject into the smallest space. In the main we agree with the opinions expressed and the advice given. A few minor mistakes appear, mostly misprints, as for instance, on page 67 the range of audition is given as from 16,000 to 50,000, when it was probably meant to state that the lower tone limit was 16; on page 70 the statement that "childhood and work in the open air predispose to inflammatory disease of the internal ear" should refer to the middle ear; and, on page 122, brain abscess is probably meant where the mortality of suppurative otitis media through "brain tumors" is spoken of. We cannot agree with the author in the limitations placed upon the use of the Eustachian

catheter. Personally, we incline to reverse his rule and use catheterization in preference to Politzerization whenever possible; the method is cleaner and the results more accurate.

We are very much gratified to note the endorsement given to the employment of formaldehyde in the treatment of suppurative otitis. Since reporting our own work with this agent we have continued to employ it in the majority of both acute and chronic cases with increasing satisfaction. Considerable space is devoted to the surgical treatment of diseases of the ear, especially for the cure of chronic suppurative conditions, all of which we heartily endorse. The importance of removing such foci of danger and thus avoiding the possibility of intracranial complications is well set forth, the indications for operation are pointed out and the methods of operating clearly described.

H. O. R.

Atlas and Epitome of Special Pathologic Histology. Vol. II. By DOCENT DR. HERMANN DÜRCK, Assistant in the Pathologic Institute in Munich. Authorized translation from the German. Edited by LUDVIG HEKTOEN, M. D. With 123 illustrations on 60 lithographic plates. (*Philadelphia and London: W. B. Saunders & Co., 1901.*)

No adverse criticism of this book seems to be justified. It is a compact book, well printed on good paper and full of colored illustrations which are really illustrative of the lesions they are intended to represent. These illustrations are drawn with care and clearness such as to make them immeasurably superior to the pictures in some of our recent American publications. The text is in places very concise and inadequate but for the great part it is written in a clear, fluent, literary style which leaves the student with a definite idea of the changes described and with energy to read more.

As the title indicates, the scope of the work is limited to the description of histological changes, but notwithstanding this fact it forms a book which ought to rank in the estimation of the student at least as high as any text-book of pathology published in English.

An American Text-Book of Pathology. Edited by LUDVIG HEKTOEN, M. D., Professor of Pathology, Rush Medical College, Chicago; and DAVID RIESMAN, M. D., Professor of Clinical Medicine, Philadelphia Polyclinic. 8vo. volume of 1245 pages and 443 illustrations. Cloth, $7.50 net. (*Philadelphia and London: W. B. Saunders & Co., 1901.*)

It is of course to be expected that a large volume treating of Pathology in general, and written in chapters by a number of different men, would be very uneven in its value from chapter to chapter. This general statement is well borne out in the book before us. It is divided into two parts, in the first of which several chapters treat of general pathology while in the second many more chapters treat of special pathology. It is impossible to enter into a detailed criticism of the work. The introduction is in the form of a general discussion of health and disease and touches on most of the fundamental principles of biology, concluding with some general advice to the student. Its lofty tone is in rather marked contrast with the rest of the book, many chapters of which seem to have been written in a perfunctory way, subjects being treated as if merely in fulfilment of the contract.

The chapters on general morbid processes, the osseous system, and the ductless glands are uniformly scholarly and are gracefully written. The difficult subject of tumors in general is treated in a thorough and comprehensive way and the relative values of the various theories with regard to them are carefully weighed. Objection may be raised to the use of the name placentoma to describe those tumors to which so many names have been applied.

Teratology is presented clearly and in an interesting way, although it seems that the use of the terms genus and species in classifying various malformations is by no means justified since they are not in any way analogous to genera and species as the terms are ordinarily used. The illustrations in this chapter are good.

The discussion of leukæmia and Hodgkin's disease is very unsatisfactory and will probably be influenced in another edition of the book by the more recent literature.

The chapter on the digestive system is distinctly below the standard maintained in some other parts of the book. It seems to be based on a rather limited acquaintance with the literature—the Montreal Medical Journal seeming to be the principal source of information—but in spite of this, wide generalizations and classifications of the most unstable type are introduced. In places the author is also rather obscure as, for example, when he says that the omentum "being a variable organ at least almost absent, was looked upon as of comparatively little use." He then describes it as a "sort of nervous heart in the abdominal cavity which keeps up an imperfect form of circulation," and further leans to the idea that it is "useful to preserve the innate heat of the body."

The illustrations throughout the book are wretched—especially is this true of the colored drawings and many of the zinc plate reproductions, from which absolutely no idea of the real appearance of the lesions is obtained. The colored drawings for example on pp. 796, 866, 933, 947 are completely valueless. Photographs of gross specimens where they are used are of course good and there are many fairly good cuts copied from other works. The book is marred throughout by the grotesque spelling which has recently been affected by certain non-literary American medical publishers.

On the whole, although there are many good chapters, some being really admirable, it seems a pity that with such an expenditure of energy the book has not made any real advance over others already on the market.

Outlines of Physiology. By EDWARD GROVES JONES, M. D., Lecturer on Physical Diagnosis in the Atlanta College of Physicians and Surgeons, and Professor of Physiology in the Dental Department of the same. With 107 illustrations. 12mo., 400 pages. Price, $1.50 net. (*Published by P. Blakiston's Son & Co., 1012 Walnut St., Philadelphia.*)

"This volume has been prepared with the view of presenting in as convenient form as possible the essential facts of modern physiology as related to the practice of medicine. In the execution of this purpose brevity has been made a prime consideration."

The four hundred pages of subject matter are divided into eleven chapters. Many of these are quite good. This applies especially to the chapters dealing with the cell (written by Dr. Frank K. Boland) and with nutrition. Occasional misstatements occur in these chapters but they fade into insignificance when compared with those that occur in some of the other chapters, especially those dealing with the chemical composition of the animal body and the senses. The author's attempt to bring the terminology of chemistry taught by our grandfathers into relation with modern chemical terms is probably the weakest feature of the work.

It is difficult to discover the place this book is to occupy. So far as brevity, "the prime consideration," is concerned we have already several text-books of physiology much more condensed than this four hundred page volume. And few of these brief text-books can boast of the inaccuracies that stud the

pages of the volume under consideration. It is to be hoped that a revision of the book will soon be undertaken, for it would give the author an opportunity of culling out the errors and of bringing the chemistry abreast of the times. This would make the book of greater value to the class of students for whom it evidently is intended.

A Practical Guide to the Administration of Anesthetics. By R. J. PROBYN-WILLIAMS, M. D., Senior Anesthetist and Instructor in Anesthetics at the London Hospital. (*London, New York and Bombay: Longmans, Green & Co., 1901.*)

This handy book of 200 pages is indeed all that its author intended it to be. It is well arranged, containing chapters on the "General Consideration of the Administration of an Anesthetic," "Difficulties and Dangers of Anesthesia," "Choice of the Anesthetic," and separate chapters devoted to nitrous oxide, ether, chloroform, and the mixtures, and on local anesthesia.

The chapter on ether is especially commendable, giving as it does all the main features of ether narcosis and the various phenomena that are likely to present themselves. We agree with the author in the stand he takes against the "open" method of administration as compared with the closed system, although we must confess that our experience with the latter method has been somewhat limited.

Nitrous oxide is fully considered but not given as wide a scope as we think possible. The writer does not tell us of its use along with air in prolonged and occasionally in even major operations. We think that this combination will become more popular and will be used more extensively in the longer surgical procedures, especially in very weak and ill patients with whom the strain of ether narcosis or the possible dangers of chloroform are to be avoided.

We regret that ethyl-bromide and chloride have not been mentioned as general anesthetics—not that we sanction their employment but that a few words on the author's experience with their use would be appreciated.

Considered as a whole, the book is clearly and concisely written and gives the reader as definite conceptions of the subject as reading matter can. It certainly must prove invaluable to students as it supplies "all the essential points in as small a form as possible." MAURICE RUBEL.

Directions for Class Work in Practical Physiology, Elementary Physiology of Muscle and Nerve and of the Vascular and Nervous Systems. By E. A. SCHÄFER, LL. D., F. R. S., Professor of Physiology in the University of Edinburgh; formerly Jodrell Professor of Physiology in University College, London. With diagrams. (*New York, London and Bombay: Longmans, Green & Co., 1901.*)

This little book of seventy-five pages contains directions which are "based upon an experience of many years in University College, London," and which have been "printed for the convenience of" Prof. Schäfer's "Edinburgh students."

As is usually the case with most laboratory manuals in physiology, this book deals almost exclusively with the physiology of muscle and nerve. The physiology of the vascular and nervous systems, the only other subjects considered, occupy but one-fifth of the book. However, the subject is handled with such simplicity and clearness as to make it quite certain that students will find it of considerable assistance to them in laboratory work. The most important features are the rough and ready character of the apparatus described, the lucidity of the numerous diagrams and the good judgment displayed in the choice of the experiments. These points may make the book of aid to teachers of physiology in planning laboratory courses.

## BOOKS RECEIVED.

*Essentials of Physiology.* Prepared especially for Students of Medicine. By Sidney P. Budgett, M. D. Arranged with Questions following each Chapter. Illustrated. (Saunders' Question-Compends, No. 1.) 1901. 12mo. 233 pages. W. B. Saunders & Company, Philadelphia and London.

*Outlines of Anatomy.* A guide to the Methodical Study of the Human Body in the Dissecting Room. By Edmund W. Holmes, A. B., M. D. Second edition. 1902. 16mo. 181 pages. The New Era Printing Company, Lancaster, Pa.

*"First Aid" to the Injured and Sick.* An Ambulance Handbook. By F. J. Warwick, B. A., M. B. Cantab., M. R. C. S., L. S. A., and A. C. Tunstall, M. D., F. R. C. S. Ed. 1901. 16mo. 239 pages. W. B. Saunders & Company, Philadelphia and London.

*Atlas and Principles of Bacteriology and Text-Book of Special Bacteriologic Diagnosis.* By Prof. Dr. K. B. Lehmann and R. O. Neumann, Dr. Phil. and Med. Authorized translation from the second enlarged and revised German edition. Edited by George H. Weaver, M. D. In two volumes. Part I, Atlas. Part II, Text. 1901. 12mo. W. B. Saunders & Company, Philadelphia and London.

*A Laboratory Course in Bacteriology.* For the use of Medical, Agricultural and Industrial Students. By Frederic P. Gorham, A. M. With 97 illustrations. 1901. 8vo. 192 pages. W. B. Saunders & Company, Philadelphia and London.

*A Text-Book of Pharmacology and Some Allied Sciences.* (Therapeutics, Materia Medica, Pharmacy, Prescription-Writing, Toxicology, etc.) By Torald Sollmann, M. D. Illustrated. 1901. 8vo. 894 pages. W. B. Saunders & Company, Philadelphia and London.

*The Principles of Hygiene.* A Practical Manual for Students, Physicians and Health Officers. By D. H. Bergey, A. M., M. D. Illustrated. 1901. 8vo. 495 pages. W. B. Saunders & Company, Philadelphia and London.

*An American Text-Book of Pathology.* For the use of Students and Practitioners of Medicine and Surgery. Edited by Ludvig Hektoen, M. D., and David Riesman, M. D. With 443 illustrations, 66 of them in colors. 1902. 4to. 1245 pages. W. B. Saunders & Company, Philadelphia and London.

*Nothnagel's Encyclopedia of Practical Medicine.* Variola, Vaccination, Varicella, Cholera, Erysipelas, Whooping Cough, Hay Fever. By H. Immermann, Th. von Jurgensen, C. Liebermeister, H. Lenhartz, G. Sticker. Edited, with additions by John W. Moore, M. D., F. R. C. P. Authorized translation from the German, under the editorial supervision of Alfred Stengel, M. D. 1902. 8vo. 682 pages. W. B. Saunders & Company, Philadelphia and London.

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